

U.S. DEPARTMENT OF COMMERCE
National Technical Information Service

PB-296 785

Endrin: Ambient Water Quality Criteria

(U.S.) Environmental Protection Agency, Washington, DC

1978

100
PB 296785

ENDRIN

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
U.S. Environmental Protection Agency
Washington, D.C.

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NATIONAL TECHNICAL
INFORMATION SERVICE
U. S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

BIBLIOGRAPHIC INFORMATION

PB-296 785

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Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for endrin.

KEYWORDS: *Water quality, *Toxicology, *Endrin, *Toxic substances, *Water pollution effects(Humans).

Available from the National Technical Information Service,
Springfield, Va. 22161

PRICE CODE: PC A06/MF A01

CRITERION DOCUMENT

ENDRIN

CRITERION

Aquatic Life

For endrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0020 µg/l as a 24-hour average and the concentration should not exceed 0.10 µg/l at any time.

For endrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0047 µg/l as a 24-hour average and the concentration should not exceed 0.031 µg/l at any time.

Human Health

For the protection of human health from the toxic properties of endrin ingested through water and contaminated aquatic organisms, the ambient water criterion is determined to be 1 ug/l.

Introduction

Endrin is the common name of one member of the cyclodiene group of pesticides. It is a cyclic hydrocarbon having a chlorine-substituted methano bridge structure. Endrin was introduced into the United States in 1951. The endrin sold in the United States is a technical grade product, containing not less than 95 percent active ingredient, available in a variety of diluted formulations. Jarvinen and Tyo (1978) found the solubility of endrin to be about 200 $\mu\text{g/l}$.

Known uses of endrin in the United States are as an avicide, rodenticide, and insecticide, the latter being the most prevalent. The largest single use of endrin domestically is for the control of lepidopteron larvae attacking cotton crops in the southeastern and Mississippi delta states. Its persistence in soil led to its discontinuation for control of tobacco worms. Thus, endrin enters the environment primarily as a result of direct applications to soil and crops. Waste material discharge from endrin manufacturing and formulating plants and disposal of empty containers also contribute significantly to observed residue levels. In the past several years, endrin utilization has been increasingly restricted and production has continued to decline. In 1978, endrin production was approximately 400,000 lbs. (U.S. EPA, 1978).

In the aquatic environment endrin is acutely toxic to carp at 0.046 $\mu\text{g/l}$ (Iyatomi, et al. 1958) and to the pink shrimp at 0.037 $\mu\text{g/l}$ (Schimmel, et al. 1975). It is chronically toxic to the fathead minnow at 0.187 $\mu\text{g/l}$ (Jarvinen and Tyo, In Press) and at .038 $\mu\text{g/l}$ to the grass shrimp

(Tyler-Schroeder, In Press). Endrin has been reported to bioconcentrate by factors as high as 15,000 in freshwater fish (Hermanutz, 1978) and 6,400 in marine fish (Hansen, et al. 1977).

Endrin is toxic to mammals, but a no-effect level of 1 mg/kg for the rat and the dog has been established by Brooks (1974). Quantitative data on endrin toxicity to humans are not available.

REFERENCES

Brooks, G.T. 1974. Chlorinated insecticides. Vol. II: Biological and environmental aspects. CRC Press, Cleveland, Ohio.

Hansen, D.J., et al. 1977. Endrin: Effects on the entire life-cycle of saltwater fish, Cyprinodon variegatus. Jour. Toxicol. Environ. Health 3: 721.

Hermanutz, R. 1978. Endrin and malathion toxicity to flagfish, Jordanella floridae. Arch. Environ. Contam. Toxicol. 7: 159.

Iyatomi, K.T., et al. 1958. Toxicity of endrin to fish. Prog. Fish. Cult. 20: 155.

Jarvinen, A.W., and R.M. Tyo. Toxicity of fathead minnows of endrin in food and water. Arch. Environ. Contam. Toxicol. 7: 1 (In press).

Schimmel, S.C, et al. 1975. Endrin: Effects on several estuarine organisms. Proc. 28th Annu. Conf. S.E. Assoc. Game and Fish Comm., 1974. p. 187.

Tyler-Schroeder, D.B. Use of grass shrimp, Palaemonetes pugio, in a life-cycle toxicity test. In Proceedings of a Symposium on Aquatic Toxicology and Hazard Evaluation. L.L. Marking and R.A. Kimerle, eds. Am. Soc. Testing and Materials (ASTM), October 31-November 1, 1977. (in press).

U.S. EPA. 1978. Endrin-Position Document 2/3. Special Pesticide Review Division. Office of Pesticide Programs, Washington, D.C.

AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Endrin is one of a group of chlorinated hydrocarbon pesticides developed after the broad scale use of DDT and its use grew during the 1950s. Perhaps because endrin has a high acute toxicity to aquatic organisms, it was more frequently tested in aquatic toxicity tests than related insecticides such as chlordane, heptachlor and aldrin.

Since it is a broad spectrum pesticide, endrin was used to control many pests including termites, mice, and army worms. In the latter 1960's it was extensively used for cotton boll worm control. Its persistence in soil, while good for termite control, led to its discontinuation for tobacco worms. Early testing identified its high toxicity to mammals.

Endrin is very insoluble in water. Recently, Jarvinen and Tyo (1978) used a saturator in their toxicity tests and found the solubility in water to be about 200 µg/l. Nearly all of the

*The reader is referred to the Guidelines for Deriving Water Quality Criteria or the Protection of Aquatic life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

early work with endrin and aquatic animals used acetone or some other solvent and in those few tests where concentrations were measured; the actual concentrations may have been considerably lower than the calculated ones. Some workers used a wetting agent such as Triton X-100 in the acetone-endrin solution to improve dispersion in the test water.

Because only acetone was used in many of the tests and because concentrations were not measured, the toxicity data reported most probably underestimate the true toxicity. There is no way to quantify this effect but the adjustment factors for unmeasured concentrations as described in the Guidelines are the best estimates that can be made at this time.

Because of the difficulty of dissolving endrin in water, data from the flow-through tests that have been conducted in which concentrations were not measured may be less reliable than data from good static tests. Recent as well as some earlier studies used measured concentrations and these data provide a reference point from which to evaluate other data.

Ferguson and co-workers at Mississippi State University have published numerous articles on endrin resistance that developed in populations of aquatic organisms exposed to high water concentrations of endrin as a result of its use for cotton. Nearly all of their work used static, unmeasured test procedures and the data, at best, can be used for relative toxicity purposes. Clearly, they did demonstrate a marked increase in tolerance to endrin of a variety of species. None of the data on

resistant populations has been included since the criterion is expected to protect unacclimated populations as well as others.

Acute Toxicity

Table 1 lists 41 data points for acute toxicity of endrin to freshwater fish. Only seven of these data from four different papers were based on measured concentrations and flow-through procedures. Of the nine data points for fathead minnows, three were derived from static tests with unmeasured concentrations. The adjusted values are closer to the flow-through, measured values than the unadjusted values suggesting the appropriateness of the adjustments. No tests on other species with measured concentrations have been reported. This is due in part to the limited use of gas chromatography during the earlier work and the high toxicity which required very low detection limits which were not achievable until analytical procedures were improved.

With a few notable exceptions, especially Iyatomi et al. (1958), most of the adjusted LC50 values are between 0.2 and 1.0 $\mu\text{g}/\text{l}$ suggesting a relatively narrow range of species sensitivity. Iyatomi, et al. (1958) reported a 3,100 times range in LC50 value for carp depending on age. No other workers have found such differences due to age. By excluding that work, all other values are within a range of about 75 times. When the geometric mean of all data is divided by the species sensitivity factor (3.9), the Final Fish Acute Value of 0.10 $\mu\text{g}/\text{l}$ is obtained as an estimate of

the concentration needed to be equal to or less than the LC50 value for 95 percent of all species. Four of the 41 adjusted values are lower than 0.10 $\mu\text{g}/\text{l}$ and two of those are from the paper by Iyatomi, et al. (1958) that was discussed above. The use of the sensitivity factor, therefore, seems reasonable.

Twenty-five LC50 values have been reported for invertebrate species but 17 species have been tested. None of the 25 data were based on measured concentrations and only two are based on flow-through procedures. Most of the species tested are substantially more tolerant than fish with few exceptions. Glass shrimp and stoneflies are comparable to fishes in sensitivity. Daphnia magna is among the more tolerant. The generally higher tolerance of the insects and related groups is unexpected since endrin is such an effective insecticide.

When the geometric mean LC50 value is divided by the species sensitivity factor (21), the Final Invertebrate Value (0.30 $\mu\text{g}/\text{l}$) is higher than only 3 of the 25 in the table, suggesting an appropriate adjustment.

The Final Acute Value is based upon the Final Fish Acute Value of 0.1 $\mu\text{g}/\text{l}$.

Chronic Toxicity

Life-cycle chronic tests have been completed with fathead minnows and flagfish giving chronic values of 0.187 and 0.257 $\mu\text{g}/\text{l}$, respectively (Table 3). Mount (1962), working with the bluntnose minnow, a species closely related to the fathead minnow, found a no observed effect concentration between 0.1

and 0.4 µg/l (Table 6). Spawning did not occur in this test but the test extended for 291 days and the results are consistent with those for the fathead minnow.

Endrin seems to enter the body rapidly as indicated by the short time for the tissues to reach equilibrium with the water (Jarvinen and Tyo, 1978). The short biological half-life, as observed by Jackson (1976) (Table 6), demonstrates that endrin is different from related pesticides such as DDT. Jarvinen and Tyo (1978) observed metabolites of endrin in the tissues of their test fish suggesting an important rate of degradation as well as elimination.

Jarvinen and Tyo (1978) also demonstrated that: (1) when food is contaminated with endrin, the toxicity of endrin in the water is greater than when uncontaminated food is fed; (2) the contribution of endrin to the body burden by food is only 10 to 15 percent of that contributed by water; and (3) residues contributed by food were additive to those contributed by water. Unfortunately, the existing data base is not sufficient to make a precise allowance for exposure through both routes for various species.

The difference between the concentrations in water that cause acute and chronic effects is small. Mount (1962) cited a reference in which the difference between acute and chronic effect levels for pheasants was small as was true with the bluntnose minnows. In Table 3, one can see the same indication

as shown by the large geometric mean application factor (0.37).

When the geometric mean chronic value is divided by the species sensitivity factor (6.7), the 95 percent value is 0.033 $\mu\text{g/l}$ which is about 30 percent of the estimate of the chronic value (0.09 $\mu\text{g/l}$) using the application factor and the Final Fish Acute Value.

No chronic data for invertebrate species were found. This deficiency may not be serious, since, based upon the acute data in Tables 1 and 2, invertebrate species are less sensitive than fish.

Plant Effects

Data on the toxicity of endrin to five species of algae are listed in Table 4. Apparently, algae are not sensitive to endrin, and the lowest value is 475 $\mu\text{g/l}$ for growth inhibition of Anacystis nidularas.

Residues

Steady-state bioconcentration factors (BCF) have been measured for nine species of organisms including algae, mussels, and fish. The geometric mean of these factors is 1,200. Table 5 also shows effect levels from feeding endrin residues to various organisms. The lowest effect level is the FDA guideline (0.03 mg/kg) for animal feed. Therefore, the Residue Limited Toxicant Concentration is 0.03 mg/kg divided by the highest BCF for a fish species of 15,000 or 0.0020 $\mu\text{g/l}$.

Miscellaneous

Table 6, containing data for other effects not listed in the first five tables, does not indicate any significant effect levels that would alter the conclusions discussed previously.

CRITERION FORMULATION

Freshwater Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 0.10 $\mu\text{g/l}$

Final Invertebrate Acute Value = 0.30 $\mu\text{g/l}$

Final Acute Value = 0.10 $\mu\text{g/l}$

Final Fish Chronic Value = 0.033 $\mu\text{g/l}$

Final Invertebrate Chronic Value = not available

Final Plant Value = 480 $\mu\text{g/l}$

Residue Limited Toxicant Concentration = 0.0020 $\mu\text{g/l}$

Final Chronic Value = 0.0020 $\mu\text{g/l}$

$0.44 \times \text{Final Acute Value} = 0.044 \mu\text{g/l}$

The maximum concentration of endrin is the Final Acute Value of 0.10 $\mu\text{g/l}$ and the 24-hour average concentration is the Final Chronic Value of 0.0020 $\mu\text{g/l}$. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For endrin the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.0020 $\mu\text{g/l}$ as a 24-hour average and the concentration should not exceed 0.10 $\mu\text{g/l}$ at any time.

Table 1. Freshwater fish acute values for endrin

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Coho salmon, <u>Oncorhynchus kisutch</u>	S	U	96	0.51	0.28	Katz, 1961
Coho salmon, <u>Oncorhynchus kisutch</u>	S	U	96	0.27	0.15	Katz & Chadwick, 1961
Coho salmon, <u>Oncorhynchus kisutch</u>	S	U	96	0.76	0.42	Post & Schroeder, 1971
Chinook salmon, <u>Oncorhynchus tshawytscha</u>	S	U	96	1.2	0.66	Katz, 1961
Chinook salmon, <u>Oncorhynchus tshawytscha</u>	S	U	96	0.92	0.50	Katz & Chadwick, 1961
Cutthroat trout, <u>Salmo clarki</u>	S	U	96	0.113	0.06	Post & Schroeder, 1971
Cutthroat trout, <u>Salmo clarki</u>	S	U	96	0.192	0.11	Post & Schroeder, 1971
Rainbow trout, <u>Salmo gairdneri</u>	S	U	96	0.405	0.22	Post & Schroeder, 1971
Rainbow trout, <u>Salmo gairdneri</u>	S	U	96	1.1	0.60	Macek, et al. 1969
Rainbow trout, <u>Salmo gairdneri</u>	S	U	96	0.58	0.32	Katz, 1961
Rainbow trout, <u>Salmo gairdneri</u>	S	U	96	0.9	0.49	Katz & Chadwick, 1961
Brook trout, <u>Salvelinus fontinalis</u>	S	U	96	0.355	0.19	Post & Schroeder, 1971
Brook trout, <u>Salvelinus fontinalis</u>	S	U	96	0.59	0.32	Post & Schroeder, 1971
Goldfish, <u>Carassius auratus</u>	S	U	48	2.0	0.89	Iyatomi, et al. 1958
Goldfish, <u>Carassius auratus</u>	S	U	96	2.1	1.15	Henderson, et al. 1959

Table 1. (Continued)

Organism	Bioassay Method**	Test Conc.	Time hrs	LC50 mg/l	Adjusted LC50 mg/l	Reference
Carp, <u>Cyprinus carpio</u>	S	U	48	140.00	61.99	Iyatomi, et al. 1958
Carp, <u>Cyprinus carpio</u>	S	U	48	6.0	2.66	Iyatomi, et al. 1958
Carp, <u>Cyprinus carpio</u>	S	U	48	5.0	2.21	Iyatomi, et al. 1958
Carp (egg), <u>Cyprinus carpio</u>	S	U	24	19.9	7.18	Iyatomi, et al. 1958
Carp (fry), <u>Cyprinus carpio</u>	S	U	24	8.5	3.07	Iyatomi, et al. 1958
Carp (fry), <u>Cyprinus carpio</u>	S	U	24	10.7	3.86	Iyatomi, et al. 1958
Carp (fry), <u>Cyprinus carpio</u>	S	U	24	4.9	1.77	Iyatomi, et al. 1958
Carp (fry), <u>Cyprinus carpio</u>	S	U	24	4.2	1.52	Iyatomi, et al. 1958
Carp (fry), <u>Cyprinus carpio</u>	S	U	24	0.061	0.022	Iyatomi, et al. 1958
Carp (fry), <u>Cyprinus carpio</u>	S	U	24	0.046	0.017	Iyatomi, et al. 1958
Bluntnose minnow, <u>Pimephales notatus</u>	FT	U	96	0.27	0.21	Mount, 1962
Bluntnose minnow, <u>Pimephales notatus</u>	FT	U	96	0.29	0.22	Mount, 1962
Bluntnose minnow, <u>Pimephales notatus</u>	FT	U	96	0.47	0.36	Mount, 1962
Fathead minnow, <u>Pimephales promelas</u>	FT	M	96	0.50	0.50	Brungs & Bailey, 1966

Table 1. (Continued)

<u>Organism</u>	<u>Bioassay Method</u>	<u>Test Conc.</u>	<u>Time (hrs)</u>	<u>LC50 (ug/l)</u>	<u>Adjusted LC50 (ug/l)</u>	<u>Reference</u>
Fathead minnow, <u>Pimephales promelas</u>	FT	M	96	0.49	0.49	Brungs & Bailey, 1966
Fathead minnow, <u>Pimephales promelas</u>	FT	M	96	0.40	0.40	Brungs & Bailey, 1966
Fathead minnow, <u>Pimephales promelas</u>	FT	M	96	0.45	0.45	Brungs & Bailey, 1966
Fathead minnow, <u>Pimephales promelas</u>	FT	M	48	0.57	0.46	Lincer, et al. 1970
Fathead minnow, <u>Pimephales promelas</u>	S	U	48	0.77	0.34	Lincer, et al. 1970
Fathead minnow, <u>Pimephales promelas</u>	S	U	96	1.1	0.60	Henderson, et al. 1959
Fathead minnow, <u>Pimephales promelas</u>	S	U	96	1.4	0.77	Henderson, et al. 1959
Fathead minnow, <u>Pimephales promelas</u>	FT	M	96	0.26	0.26	Solon, et al. 1969
Fathead minnow, <u>Pimephales promelas</u>	FT	M	96	0.85	0.85	Hermanutz, In press
Flagfish, <u>Jordaniella floridae</u>	S	U	96	0.75	0.410	Katz & Chadwick, 1961
Mosquitofish, <u>Gambusia affinis</u>	S	U	96	0.9	0.492	Katz & Chadwick, 1961
Guppy, <u>Lebistes reticulatus</u>	S	U	96	1.6	0.875	Henderson, et al. 1959
Guppy, <u>Lebistes reticulatus</u>	S	U	96	0.44	0.241	Katz, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	48	0.27	0.097	Fabacher, 1976
Largemouth bass, <u>Micropterus salmoides</u>	S	U				

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (µg/l)	Adjusted LC50 (µg/l)	Reference
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.6	0.33	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	8.25	4.51	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	5.5	3.00	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	2.4	1.31	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	1.65	0.90	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.86	0.47	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.33	0.18	Katz & Chadwick, 1961
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.61	0.33	Macek, et al. 1969
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.41	0.22	Macek, et al. 1969
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.37	0.20	Macek, et al. 1969
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.66	0.36	Henderson, et al. 1959
<u>Bluegill, Lepomis macrochirus</u>	FT	U	24	2.0	1.54	Bennett & Day, 1970
<u>Bluegill, Lepomis macrochirus</u>	S	U	96	0.61	3.34	Sanders, 1972

* S = static, FT = flow-through

** U = unmeasured, M = measured

Geometric mean of adjusted values = $0.389 \mu\text{g/l}$ $\frac{0.389}{3.9} = 0.10 \mu\text{g/l}$ Lowest value from a flow-through test with measured concentrations = $0.26 \mu\text{g/l}$

Table 2. Freshwater invertebrate acute values for endrin

Organism	Bioassay Method	Test Conc., $\mu\text{g/l}$	Time (hrs)	LC50 ($\mu\text{g/l}$)	Adjusted LC50 ($\mu\text{g/l}$)	Reference
Clam, <u>Eupera singleyi</u>	S	U	72	60	31.0	Naqvi & Ferguson, 1968
Snail, <u>Physa gyrina</u>	S	U	72	500	258.3	Naqvi & Ferguson, 1968
Cladoceran, <u>Simoccephalus serrulatus</u>	S	U	48	26	22.0	Sanders, 1966
Cladoceran, <u>Simoccephalus serrulatus</u>	S	U	48	45	38.1	Sanders, 1966
Cladoceran, <u>Daphnia magna</u>	S	U	50	352	298.1	Gauvin, et al. 1965
Copepod, <u>Cyclopoid</u>	S	U	48	60	21.9	Naqvi & Ferguson, 1968
Sowbug, <u>Asellus brevicaudus</u>	S	U	96	1.5	1.27	Sanders, 1972
Scud, <u>Gammarus fasciatus</u>	S	U	96	4.3	3.64	Sanders, 1972
Scud, <u>Gammarus fasciatus</u>	S	U	96	1.3	1.10	Sanders, 1972
Scud, <u>Gammarus fasciatus</u>	FT	U	96	5.5	4.24	Sanders, 1972
Scud, <u>Gammarus lacustris</u>	S	U	96	3.0	2.54	Sanders, 1969
Scud, <u>Gammarus lacustris</u>	S	U	96	11.5	9.74	Nebeker & Gauvin, 1964
Glass shrimp, <u>Palaeomonetes kadiakensis</u>	S	U	96	3.2	2.71	Sanders, 1972
Glass shrimp, <u>Palaeomonetes kadiakensis</u>	FT	U	96	0.5	0.39	Sanders, 1972
Glass shrimp, <u>Palaeomonetes kadiakensis</u>	S	U	24	0.9	0.20	Naqvi & Ferguson, 1970

Table 2. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Crayfish, <u>Orconectes nais</u>	S	U	96	320	271.0	Sanders, 1972
Crayfish, <u>Orconectes nais</u>	S	U	96	3.2	2.71	Sanders, 1972
Mayfly, <u>Hexagenia bilineata</u>	S	U	96	64	54.2	Sanders, 1972
Mayfly, <u>Ephemera grandis</u>	S	U	96	4.7	3.98	Gauvin, et al. 1965
Stonefly, <u>Acroneuria pacifica</u>	S	U	96	0.32	0.27	Jensen & Gauvin, 1966
Stonefly, <u>Pteronarcys californica</u>	S	U	96	2.4	2.03	Jensen & Gauvin, 1966
Stonefly, <u>Pteronarcys californica</u>	S	U	96	0.25	0.21	Sanders & Cope, 1968
Stonefly, <u>Pteronarcella badia</u>	S	U	96	0.54	0.46	Sanders & Cope, 1968
Stonefly, <u>Claassenia sabulosa</u>	S	U	96	0.76	0.64	Sanders & Cope, 1968
Damselfly, <u>Ischnura verticalis</u>	S	U	96	1.8	1.53	Sanders, 1972

* S = static, FT = flow-through

** U = unmeasured

Geometric mean of adjusted values = 6.22 ug/l $\frac{6.22}{21} = 0.30$ ug/l

Table 3. Freshwater fish chronic values* for endrin

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)	Reference
Fathead minnow, <u>Pimephales promelas</u>	LC	0.14-0.25	0.187	Jarvinen & Tyo, 1978
Flagfish, <u>Jordanelia floridae</u>	LC	0.22-0.3	0.257	Hermanutz, 1978

* LC = life cycle or partial life cycle

Geometric mean of chronic values = 0.219 ug/l $\frac{0.219}{6.7} = 0.033 \text{ ug/l}$

Lowest chronic value = 0.187 ug/l

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Species	Application Factor Values			Reference
	96-hr LC50 (ug/l)	MATC (ug/l)	AF	
Fathead minnow, <u>Pimephales promelas</u>	0.409*	0.187	0.46	Jarvinen & Tyo, 1978
Flagfish, <u>Jordanelia floridae</u>	0.85	0.257	0.30	Hermanutz, 1978
Geometric mean AF = 0.37			Geometric mean LC50 = 0.59 ug/l	
0.37			$\sqrt{0.1 \times 0.59} = 0.09 \text{ ug/l}$	

* Since Jarvinen and Tyo (1978) did not provide a 96-hr LC50 value, the geometric mean of six 96-hr LC50 values (for flow through tests with measured concentrations) was used as an estimate of the LC50 for calculating an AF for fathead minnows.

Table 4. Freshwater plant effects for endrin

<u>Organism</u>	<u>Effect</u>	<u>Concentration</u> ($\mu\text{g/l}$)	<u>Reference</u>
Alga, <u>Anacystis nidularia</u>	growth	475	Batterton, 1971
Alga, <u>Microcystis aeruginosa</u>	growth	>1,000 <5,000	Vance & Drummond, 1969
Alga, <u>Anabaena cylindrica</u>	growth	>15,000	Vance & Drummond, 1969
Alga, <u>Scenedesmus quadricauda</u>	growth	>20,000	Vance & Drummond, 1969
Alga, <u>Oedogonium sp.</u>	growth	>20,000	Vance & Drummond, 1969

Lowest plant value = 475 $\mu\text{g/l}$

Table 5. Freshwater residues for endrin

<u>Organism</u>	<u>Bioconcentration Factor</u>	<u>Time (days)</u>	<u>Reference</u>
Alga, <u>Microcystis aeruginosa</u>	200	7	Vance & Drummond, 1969
Alga, <u>Anabaena cylindrica</u>	222	7	Vance & Drummond, 1969
Alga, <u>Scenedesmus quadricauda</u>	156	7	Vance & Drummond, 1969
Alga, <u>Oedogonium</u> sp.	140	7	Vance & Drummond, 1969
Mussels, (Mixed species)	3,000	21	Jarvinen & Tyo, 1978
Fathead minnow, <u>Pimephales promelas</u>	10,000	47	Mount & Putnicki, 1966
Fathead minnow, <u>Pimephales promelas</u>	7,000	300	Jarvinen & Tyo, 1978
Channel catfish, <u>Ictalurus punctatus</u>	2,000 1,640	41 55	Argyle, et al. 1973
Flagfish, <u>Jordanella floridae</u>	15,000	65	Hermanutz, 1978

<u>Organism</u>	<u>Action Level or Effect</u>	<u>Concentration (mg/kg)</u>	<u>Reference</u>
Man	edible fish and shellfish	0.3	U.S. FDA Admin. Guideline 7420.09, 1973
Domestic animals	animal feed	0.03	U.S. FDA Admin. Guideline 7426.04, 1974
Rainbow trout, <u>Salmo gairdneri</u>	osmoregulation	0.725	Grant & Mehrle, 1973
Goldfish, <u>Carassius auratus</u>	growth inhibition	0.43	Grant & Mehrle, 1970
Fathead minnow, <u>Pimephales promelas</u>	reduced survival	0.63	Jarvinen & Tyo, 1978

Table 5. (Continued)

Geometric mean bioconcentration factor for all species = 1,200
 Highest bioconcentration factor for a single fish species = 15,000
 For FDA animal feed: $\frac{0.03 \text{ mg/kg}}{15,000} = 0.0000020 \text{ mg/kg}$ or $0.0020 \text{ } \mu\text{g/l}$
 For effect on wildlife: $\frac{0.43}{1,200} = 0.00036 \text{ mg/kg}$ or $0.36 \text{ } \mu\text{g/l}$

Table 6. Other freshwater data for endrin

<u>Organism</u>	<u>Test Duration</u>	<u>Effect</u>	<u>Result (ug/l)</u>	<u>Reference</u>
Rainbow trout, <u>Salmo gairdneri</u>	15 min	ATPase inhibition	10 ⁻⁴ molar	Davis, et al. 1972
Golden shiner, <u>Notemigonus crysoleucas</u>	36 hrs	LC50	2.0	Ludke, et al. 1968
Bluntnose minnow, <u>Pimephales notatus</u>	291 days	Growth inhibition	0.4	Mount, 1962
Channel catfish, <u>Ictalurus punctatus</u>	12 days	Half life of residue	-	Jackson, 1976
Yellow bullhead, <u>Ictalurus natalis</u>	36 hrs	LC50	1.25	Ferguson & Bingham, 1966
Black bullhead, <u>Ictalurus melas</u>	36 hrs	LC50	0.37	Ferguson, et al. 1965
Mosquitofish, <u>Gambusia affinis</u>	36 hrs	LC50	1.0	Ferguson, et al. 1966
Largemouth bass, <u>Micropterus salmoides</u>	20 days	LC20	0.1	Fabacher, 1976
Bluegill, <u>Lepomis macrochirus</u>	-	Weak inhibition of Mg ²⁺ and Na ⁺ -K ⁺ ATPase	41.7 μ M	Cutkomp, et al. 1971
Stonefly, <u>Pteronarcys californica</u>	30 days	LC50	1.2	Jensen & Gauffin, 1966
Stonefly, <u>Acroneuria pacifica</u>	30 days	LC50	0.035	Jensen & Gauffin, 1966

Lowest value = 0.035 μ g/l

SALTWATER ORGANISMS

Introduction

The acute toxicity of endrin to saltwater organisms has been relatively well studied particularly in the 1960's, probably because it has been used widely and has proven to be one of the most acutely toxic insecticides. Data on bioaccumulation of endrin and its chronic toxicity have been available only recently. Although the criterion for endrin is based on its bioconcentration, acute and chronic toxicity to invertebrate species is only slightly above the Final Chronic Value. The similarity of these values is significant because only slight excursions above an acceptable concentration of endrin in water may result in acute toxicity or unacceptable accumulation in seafood consumed by man.

Acute Toxicity

Acute toxicity tests have been conducted with seventeen species of saltwater fishes and sensitivity varies considerably (Table 7). Adjusted LC50 values ranged from 0.026 $\mu\text{g/l}$ for chinook salmon (Schoettger, 1970) to 1.7 $\mu\text{g/l}$ for northern puffer (Eisler, 1970b). Only two, usually tolerant, species, the sheepshead minnow (Hansen, et al. 1977) and the sailfin molly (Schimmel, et al. 1975) have been tested for 96-hours in flow-through tests with measured endrin concentrations. Sheepshead minnow fry, juveniles, and adults did not differ in their sensitivity to acute exposure to endrin (Hansen, et al. 1977). Fifteen species of freshwater fishes, excluding carp, were as sensitive as saltwater fishes; adjusted LC50 values ranged from 0.06 to 4.51 $\mu\text{g/l}$ (Table 1).

Acute toxicity tests with saltwater invertebrate species also demonstrate that endrin is very toxic (Table 8). The variability in adjusted LC50 or EC50 values is greater than that for fishes, ranging from 0.037 to 670 $\mu\text{g}/\text{l}$. Unlike most insecticides, the sensitivity of arthropods to endrin is not much different from the sensitivity of fishes. The penaeid shrimp were the most sensitive species tested, with adjusted LC50 values from 0.037 to 0.099 $\mu\text{g}/\text{l}$ (Schimmel, et al. 1975; Lowe, unpublished; and Butler, 1963). Adjusted LC50 values of five other arthropod species ranged from 0.23 $\mu\text{g}/\text{l}$ for Korean shrimp (Schoettger, 1970) to 8.3 $\mu\text{g}/\text{l}$ for blue crabs (Butler, 1963). The sensitivity of different life-stages of grass shrimp is similar, differing by only a factor of 3.4 (Tyler-Schroeder, In press). American oysters were less sensitive than arthropods, with adjusted EC50 values, based on decreased shell deposition or abnormal development of larvae, ranging from 14.2 to 670 $\mu\text{g}/\text{l}$ (Table 8). The toxicity of endrin to oysters may be directly related to water temperature. The range in adjusted LC50 values for 17 species of freshwater mollusks and arthropods (0.20 to 298 $\mu\text{g}/\text{l}$; Table 2) was almost as great as the range for saltwater species but none was as sensitive as penaeid shrimp.

Data on LC50 values for fishes and invertebrate species in acute toxicity tests with endrin support the hypothesis that the acute toxicity of endrin is underestimated by static tests and by not measuring concentrations of endrin in test water. Therefore, LC50 values must be adjusted for test conditions if relative

species sensitivity is to be understood. For the same tests, LC50 or EC50 values based on nominal concentrations for sheepshead minnows ($0.40 \mu\text{g/l}$), sailfin mollies ($0.79 \mu\text{g/l}$), grass shrimp ($0.73 \mu\text{g/l}$), pink shrimp ($0.049 \mu\text{g/l}$), and American oysters ($19.1 \mu\text{g/l}$) were higher than LC50 or EC50 values for measured concentrations (Table 7; Schimmel, et al. 1975). Additionally, LC50 values based on static tests were greater than LC50 values for flowthrough tests of the same duration for shiner perch, dwarf perch, Korean shrimp, and grass shrimp (Earnest and Benville, 1972; Schoettger, 1970; Tyler-Schroeder, In press; Schimmel, et al. 1975; Eisler, 1969). The greater variability in sensitivity of invertebrate species to endrin than was observed for fishes supports the need for a higher species sensitivity factor for invertebrate species.

The Final Acute Values of fish and invertebrate species are similar. The Final Fish Acute Value, obtained by dividing the geometric mean of the adjusted LC50 values ($0.209 \mu\text{g/l}$) by the species sensitivity factor (3.7), is $0.056 \mu\text{g/l}$. The Final Invertebrate Acute Value, obtained by dividing the geometric mean of the adjusted LC50 values for invertebrate species ($1.5 \mu\text{g/l}$) by the species sensitivity factor (49), is $0.031 \mu\text{g/l}$. The species sensitivity factors for fish and invertebrate species seem appropriate because the adjusted LC50 values of one of 17 fishes was less than the Final Fish Acute Value and the Final Invertebrate Acute Value was slightly less than adjusted LC50 values of the most sensitive of the nine species tested. The Final Acute Value is $0.031 \mu\text{g/l}$.

Chronic Toxicity

Sheepshead minnows (Schimmel, et al. 1975; Hansen, et al. 1977), spot (Lowe, 1965), and mummichog (Eisler, 1970a) have been exposed chronically to endrin for 10 days or longer (Tables 9 and 12). Only the life-cycle exposure of sheepshead minnows (Hansen, et al. 1977) is suitable for obtaining a Final Fish Chronic Value. In this test, embryos exposed to 0.31 and 0.72 $\mu\text{g}/\text{l}$ hatched early; all fry exposed to 0.72 $\mu\text{g}/\text{l}$, and about one-half exposed to 0.31 $\mu\text{g}/\text{l}$, died. Females died during spawning, fewer eggs were fertile, and survival of exposed progeny decreased in 0.31 $\mu\text{g}/\text{l}$. No significant effects were observed on survival, growth, or reproduction at an exposure concentration of 0.12 $\mu\text{g}/\text{l}$. The MATC limits, 0.12 to 0.31 $\mu\text{g}/\text{l}$, were not much less than the 96-hour LC50, 0.34 $\mu\text{g}/\text{l}$, indicating that there is little difference between endrin concentrations that produce acute effects and ones that produce no effect in chronic tests. Life-cycle tests with the freshwater fish, fathead minnow and flagfish also show little difference between acute and chronic toxicity of endrin (Table 3). The saltwater Final Fish Chronic Value for endrin is obtained by dividing the chronic value (0.19 $\mu\text{g}/\text{l}$) by the species sensitivity factor (6.7) and is 0.028 $\mu\text{g}/\text{l}$.

An embryo-larval test with sheepshead minnows (Schimmel, et al. 1975) was not used to obtain a chronic value because only LC50 values and nominal observed no-effect concentrations were reported (Table 12). However, results were similar to those reported in the life cycle test. The LC50 value based on measured

concentrations for fry on the 33rd day of the experiment was 0.158 $\mu\text{g}/\text{l}$. Although fish exposed to a nominal concentration of 0.21 $\mu\text{g}/\text{l}$ had no significant mortality, they were visibly affected by endrin.

Fifty-seven percent of the juvenile spot were exposed to endrin at a concentration of 0.075 $\mu\text{g}/\text{l}$ within 19 days. Spot exposed to 0.05 $\mu\text{g}/\text{l}$ were apparently not affected (Lowe, 1966). Fish exposed to 0.05 $\mu\text{g}/\text{l}$ exhibited no signs of poisoning and survival, length and weight did not differ from those of control organisms. The nominal, no observed effect concentration of 0.05 $\mu\text{g}/\text{l}$ was 0.21 of the adjusted LC50 of 0.23 $\mu\text{g}/\text{l}$, and this also supports the hypothesis of a minimal difference between the acute and the chronic toxicity of endrin to fish.

The only other datum on chronic effects of endrin on a saltwater fish (Fundulus heteroclitus) show a 10-day LC50 based on nominal concentrations of 0.33 $\mu\text{g}/\text{l}$ (Eisler, 1970a), which is little different from the unadjusted 96-hour LC50 values of 0.6 and 1.5 $\mu\text{g}/\text{l}$ (Eisler, 1970b).

One saltwater invertebrate species, grass shrimp, has been exposed to endrin in a partial life-cycle toxicity test (Tyler-Schroeder, In press). Survival of the parental generation was reduced by exposure to 0.11 $\mu\text{g}/\text{l}$. Onset and duration of spawning were significantly delayed and lengthened for female grass shrimp at all exposure concentrations (0.03 to 0.79 $\mu\text{g}/\text{l}$). The number of females depositing eggs was less than that of controls, but egg

production and hatching success apparently were not affected. Larval mortality increased, time to metamorphosis increased, and growth of juvenile shrimp was decreased by endrin concentrations of 0.11 $\mu\text{g/l}$ and higher.

The Final Invertebrate Chronic Value was obtained for endrin (Table 10), even though all tested concentrations significantly impaired some life-cycle function. A lower MATC limit of 0.03 $\mu\text{g/l}$ was selected because the only effect was a delay in onset of spawning of about one week. A delay of one week probably would not affect natural populations. The upper MATC limit of 0.05 $\mu\text{g/l}$ was set on decrease in number of ovigerous females and delay in spawning of 3 to 4 weeks. The Final Invertebrate Chronic Value of 0.075 $\mu\text{g/l}$ is obtained by dividing the chronic value (0.038) by the species sensitivity factor (5.1). The species sensitivity factor is needed because grass shrimp are intermediate in their sensitivity to acute exposure to endrin, compared to other salt-water invertebrate species.

Plant Effects

Three published studies on five species of phytoplankton and a natural phytoplankton community (Table 11) indicate that effects of endrin on phytoplankton are unlikely at concentrations protective of acute effects on most invertebrate and fish species. Menzel, et al. (1970) in tests with four phytoplankton species found effects at concentrations greater than 1 $\mu\text{g/l}$. Productivity of natural phytoplankton communities was reduced by 46 percent in

1,000 $\mu\text{g}/\text{l}$ (Butler, 1963). Growth rate of Agmenellum quadruplicatum was reduced in as little as 0.2 $\mu\text{g}/\text{l}$ (Batterton, et al. 1971).

Residues

The bioconcentration of endrin from water into the tissues of saltwater organisms has been well studied (Table 12 and 13). Probable steady-state bioconcentration factors (BCF) are available from studies with American oysters (Mason and Rowe, 1976; Wilson, 1966); grass shrimp (Tyler-Schroeder, In press); sheepshead minnows (Hansen, et al. 1977); and spot (Lowe, 1966). Additional BCF data (Table 13) are available from 96-hour exposures of oysters, grass shrimp, pink shrimp, sheepshead minnows, and sailfin mollies, to endrin (Schimmel, et al. 1975).

Bioconcentration factors (Table 12) for endrin in American oysters exposed for seven days ranged from 1,670 to 2,780 (Mason and Rowe, 1976). Endrin accumulated rapidly, reaching steady-state after about 48 hours of exposure. Oysters placed in endrin-free water depurated endrin at a rate of 0.005 $\mu\text{g}/\text{g h}^{-1}$, resulting in a biological half-life of 67 hours. Based on this experiment, the oysters exposed to endrin in a flow-through test by Wilson (1966) were probably at steady-state and had a BCF of 1,000, based on a nominal water concentration. Oysters exposed for only 96 hours had an average BCF of 1,200 (Schimmel, et al. 1975).

Bioconcentration factors for endrin in grass shrimp in two experiments averaged 1,490 and 1,600 (Tyler-Schroeder, In press).

In the first experiment, steady-state was reached after 2.5 days of a 21-day exposure. Ninety percent of the endrin was depurated within 4.2 days. In the second experiment, the average BCF of endrin was 1,600 in parental generation shrimp from a partial life-cycle exposure lasting 5 months. Average bioconcentration factors after a 96-hour exposure were 830 for grass shrimp and 980 for pink shrimp (Schimmel, et al. 1975).

Bioconcentration data for two of three species of saltwater fish differs little from those for invertebrate species. Bioconcentration factors calculated from nominal water concentrations were 1,340 for spot exposed for 8 months and 1,560 for spot exposed for 5 months (Lowe, 1966). The average BCF for juvenile sheepshead minnows exposed for 28 days was 2,500, for adults exposed for 147 to 161 days the BCF was 6,400 (Hansen, et al. 1977) and for juveniles exposed 4 days the BCF was 2,600 (Schimmel, et al. 1975). Sailfin mollies exposed to endrin for four days had an average BCF of 2,400 (Schimmel, et al. 1975).

The use of data on the bioconcentration of endrin (Table 12) and on the FDA limit of 0.03 mg/kg for animal feed results in a Residue Limited Toxicant Concentration (RLTC) for endrin of 0.047 µg/l. This value is lower than the Final Fish or Invertebrate Chronic Values and the Final Plant Value and therefore the RLTC becomes the Final Chronic Value.

Miscellaneous

Other data included in the tables but not yet discussed, do not contribute significantly to the derivation of a criterion for endrin.

CRITERION FORMULATION

Saltwater Aquatic-Life

Summary of Available Data

The concentrations below have been rounded to two significant figures

Final Fish Acute Value = 0.056 $\mu\text{g/l}$

Final Invertebrate Acute Value = 0.031 $\mu\text{g/l}$

Final Acute Value = 0.031 $\mu\text{g/l}$

Final Fish Chronic Value = 0.028 $\mu\text{g/l}$

Final Invertebrate Chronic Value = 0.0075 $\mu\text{g/l}$

Final Plant Value = 0.2 $\mu\text{g/l}$

Residue Limited Toxicant Concentration = 0.0047 $\mu\text{g/l}$

Final Chronic Value = 0.0047 $\mu\text{g/l}$

0.44 x Final Acute Value = 0.014 $\mu\text{g/l}$

The maximum concentration of endrin is the Final Acute Value of 0.031 $\mu\text{g/l}$ and the 24-hour average concentration is the Final Chronic Value of 0.0047 $\mu\text{g/l}$. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For endrin the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0047 $\mu\text{g/l}$ as a 24-hour average and the concentration should not exceed 0.031 $\mu\text{g/l}$ at any time.

Table 7. Marine fish acute values for endrin

Organism	Bioassay Method	Test Conc.,**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
American eel, <u>Anguilla rostrata</u>	S	U	96	0.6	0.32	Eisler, 1970b
Gulf menhaden, <u>Brevortia patronus</u>	FT	U	24	0.80	0.41	Lowe, 1966
Chinook salmon, <u>Oncorhynchus tshawytscha</u>	S	U	96	0.048	0.026	Schoettger, 1970
Sheepshead minnow (fry), <u>Cyprinodon variegatus</u>	FT	M	96	0.37	0.37	Hansen, et al. 1977
Sheepshead minnow (juvenile), <u>Cyprinodon variegatus</u>	FT	M	96	0.34	0.34	Hansen, et al. 1977
Sheepshead minnow (adult), <u>Cyprinodon variegatus</u>	FT	M	96	0.36	0.36	Hansen, et al. 1977
Sheepshead minnow (juvenile), <u>Cyprinodon variegatus</u>	FT	M	96	0.38	0.38	Schimmel, et al. 1975
Sheepshead minnow, <u>Cyprinodon variegatus</u>	FT	U	24	0.32	0.16	Lowe, 1966
Hummichog, <u>Fundulus heteroclitus</u>	S	U	96	0.6	0.33	Eisler, 1970b
Hummichog, <u>Fundulus heteroclitus</u>	S	U	96	1.5	0.82	Eisler, 1970b
Striped killifish, <u>Fundulus majalis</u>	S	U	96	0.3	0.16	Eisler, 1970b
Longnose killifish, <u>Fundulus similis</u>	FT	U	24	0.23	0.12	Lowe, 1966
Longnose killifish, <u>Fundulus similis</u>	FT	U	48	0.3	0.19	Burley, 1963
Sailfin molly, <u>Poecilia latipinna</u>	FT	M	96	0.63	0.63	Schimmel, et al. 1975

Table 7. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Atlantic silverside, <u>Menidia menidia</u>	S	U	96	0.05	0.027	Eisler, 1970b
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	1.65	0.90	Katz & Chadwick, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	1.50	0.82	Katz & Chadwick, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	1.20	0.66	Katz & Chadwick, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	1.57	0.86	Katz & Chadwick, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	1.57	0.86	Katz & Chadwick, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	0.44	0.24	Katz, 1961
Threespine stickleback, <u>Gasterosteus aculeatus</u>	S	U	96	0.50	0.27	Katz, 1961
Striped bass, <u>Morone saxatilis</u>	FT	U	96	0.094	0.072	Korn & Earnest, 1974
Spot, <u>Leiostomus xanthurus</u>	FT	U	24	0.45	0.23	Lowe, 1966
Shiner perch, <u>Cymatogaster aggregata</u>	S	U	96	0.8	0.44	Earnest & Benville, 1972
Shiner perch, <u>Cymatogaster aggregata</u>	FT	U	96	0.12	0.09	Earnest & Benville, 1972
Dwarf perch, <u>Micrometrus minimus</u>	S	U	96	0.6	0.33	Earnest & Benville, 1972
Dwarf perch, <u>Micrometrus minimus</u>	FT	U	96	0.13	0.10	Earnest & Benville, 1972
Bluehead, <u>Thalassoma bifasciatum</u>	S	U	96	0.1	0.055	Eisler, 1970b

Table 7. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Striped mullet, <u>Mugil cephalus</u>	S	U	96	0.3	0.16	Eisler, 1970b
Striped mullet, <u>Mugil cephalus</u>	FT	U	24	2.6	1.3	Lowe, 1966
Striped mullet, <u>Mugil cephalus</u>	FT	U	48	0.4	0.25	Lowe, data sheets
Northern puffer, <u>Sphaeroides maculatus</u>	S	U	96	3.1	1.7	Eisler, 1970b

* S = static, FT = flow through

** U = unmeasured, M = measured

Geometric mean of adjusted values = $0.209 \mu\text{g/l}$ $\frac{0.209}{3.7} = 0.056 \mu\text{g/l}$ Lowest value from a flow-through test with measured concentrations = $0.34 \mu\text{g/l}$

Table 8. Marine invertebrate acute values for endrin

Organism	Bicassay Method	Test Conc. **	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
American oyster (embryo), <u>Crassostrea virginica</u>	S	U	48	790***	670	Davis & Hidu, 1969
American oyster, <u>Crassostrea virginica</u>	FT	M	96	14.2***	14.2	Schimmel, et al. 1975
American oyster, <u>Crassostrea virginica</u>	FT	U	96	33***	25.4	Butler, 1963
American oyster, <u>Crassostrea virginica</u>	FT	U	96	400***	308	Lowe, data sheets
Blue crab, <u>Callinectes sapidus</u>	FT	U	48	25	8.3	Butler, 1963
Sand shrimp, <u>Crangon septemspinosa</u>	S	U	96	1.7	1.4	Eisler, 1969
Hermit crab, <u>Pagurus longicarpus</u>	S	U	96	12	10	Eisler, 1969
Korean shrimp, <u>Palaeomon macrodactylus</u>	S	U	96	4.7	4.0	Schoettger, 1970
Korean shrimp, <u>Palaeomon macrodactylus</u>	FT	U	96	0.3	0.23	Schoettger, 1970
Grass shrimp (larva), <u>Palaeomonetes pugio</u>	FT	M	96	1.2	1.2	Tyler-Schroeder, In press
Grass shrimp (juvenile), <u>Palaeomonetes pugio</u>	FT	M	96	0.35	0.35	Tyler-Schroeder, In press
Grass shrimp (adult), <u>Palaeomonetes pugio</u>	FT	M	96	0.69	0.69	Tyler-Schroeder, In press
Grass shrimp, <u>Palaeomonetes pugio</u>	FT	M	96	0.63	0.63	Schimmel, et al. 1975
Grass shrimp, <u>Palaeomonetes pugio</u>	FT	U	48	0.8	0.26	Lowe, data sheets

Table 8. (Continued)

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Grass shrimp, <u>Palaeomonetes vulgaris</u>	S	U	96	1.8	1.5	Eisler, 1969
Pink shrimp, <u>Penaeus duorarum</u>	FT	H	96	0.037	0.037	Schimmel, et al. 1975
Pink shrimp, <u>Penaeus duorarum</u>	FT	U	48	0.2	0.066	Lowe, data sheets
Brown shrimp, <u>Penaeus aztecus</u>	FT	U	48	0.3***	0.099	Butler, 1963

* S = static, FT = flow-through

** U = unmeasured, H = measured

*** Abnormal development of oyster larvae; decreased growth of oyster; or loss of equilibrium of brown shrimp or blue crabs.

Geometric mean of adjusted values = 1.5 ug/l $\cdot \frac{1.5}{49} = 0.031 \text{ ug/l}$ Lowest value from a flow-through test with measured concentrations = 0.037 ug/l

Table 9. Marine fish chronic values for endrin.

<u>Organism</u>	<u>Test*</u>	<u>Limits</u> ($\mu\text{g/l}$)	<u>Chronic</u> <u>Value</u> ($\mu\text{g/l}$)	<u>Reference</u>
Sheepshead minnow, <u>Cyprinodon variegatus</u>	LC	0.12-0.31	0.19	Hansen, et al. 1977

* LC = life cycle or partial life cycle

Geometric mean chronic values = $0.19 \mu\text{g/l}$ $\frac{0.19}{6.7} = 0.028 \mu\text{g/l}$

Lowest chronic value = $0.19 \mu\text{g/l}$

Application Factor Values

<u>Species</u>	<u>96-hr LC50</u> ($\mu\text{g/l}$)	<u>MATC</u> ($\mu\text{g/l}$)	<u>AF</u>	<u>Reference</u>
Sheepshead minnow, <u>Cyprinodon variegatus</u>	0.34	0.12-9.31	0.56	Hansen, et al. 1977

Geometric mean AF = 0.56

Geometric mean LC50 = $0.34 \mu\text{g/l}$

$0.56 \sqrt{0.34 \mu\text{g/l} \times 0.056 \mu\text{g/l}} = 0.077 \mu\text{g/l}$

Table 10. Marine invertebrate chronic values for endrin (Tyler-Schroeder, In press)

<u>Organism</u>	<u>Test*</u>	<u>Limits</u> <u>(ug/l)</u>	<u>Chronic</u> <u>Value</u> <u>(ug/l)</u>
Grass shrimp, <u>Palaeomonetes pugio</u>	LC	0.03-0.05*	0.038

* LC = life cycle or partial life cycle

** Onset of spawning was delayed about one week in shrimp exposed to 0.03 ug/l. Because a delay of one week would probably not affect natural populations, MATC limits were set on decreases in number of ovigerous females and delayed spawning of 3-4 weeks in 0.05 ug/l of endrin.

Geometric mean of chronic values = 0.038 ug/l $\frac{0.038}{5.1} = 0.0075$ ug/l

Lowest chronic value = 0.039 ug/l

Table 11. Marine plant effects for endrin

<u>Organism</u>	<u>Effect</u>	<u>Concentration</u> ($\mu\text{g/l}$)	<u>Reference</u>
Alga, <u>Agmenellum</u> <u>quadricapitatum</u>	Growth rate inhibited	0.2, 19, 95 475, 950	Batterton, et al. 1971
Alga, <u>Dunaliella</u> <u>tertiotecta</u>	No effect on ^{14}C or cell division	1,000	Menzel, et al. 1970
Alga, <u>Skeletonema costatum</u>	^{14}C uptake reduced	>10	Menzel, et al. 1970
Alga, <u>Skeletonema costatum</u>	Growth reduced first 5 days of test	100	Menzel, et al. 1970
Alga, <u>Coccolithus huxlegi</u>	^{14}C uptake reduced	>10	Menzel, et al. 1970
Alga, <u>Coccolithus huxlegi</u>	Growth reduced	100	Menzel, et al. 1970
Alga, <u>Cyclotella nana</u>	^{14}C uptake	>1.0	Menzel, et al. 1970
Alga, <u>Cyclotella nana</u>	Growth reduced	100	Menzel, et al. 1970
Natural phytoplankton communities	46% decrease in productivity; ^{14}C	1,000	Butler, 1963

Lowest plant value = 0.2 $\mu\text{g/l}$

Table 12. Marine residues for endrin

<u>Organism</u>	<u>Bioconcentration Factor</u>	<u>Time (days)</u>	<u>reference</u>
American oyster, <u>Crassostrea virginica</u>	1,670-2,780	7	Mason & Rowe, 1976
American oyster, <u>Crassostrea virginica</u>	1,000	10	Wilson, 1966
Grass shrimp, <u>Palaemonetes pugio</u>	1,490	21	Tyler-Schroeder, In press
Grass shrimp, <u>Palaemonetes pugio</u>	1,600	145	Tyler-Schroeder, In press
Sheepshead minnow, <u>Cyprinodon variegatus</u>	2,500	28	Hansen, et al. 1977
Sheepshead minnow, <u>Cyprinodon variegatus</u>	6,400	147-161	Hansen, et al. 1977
Spot, <u>Leiostomus xanthurus</u>	1,450	5 to 10 months	Lowe, 1966

<u>Organism</u>	<u>Action Level or Effect</u>	<u>Concentration (mg/kg)</u>	<u>Reference</u>
Man	edible fish and shellfish	0.3	U.S. FDA Admin. Guideline - 7420.09, 1973
Domestic animals	animal feed	0.03	U.S. FDA Admin. Guideline - 7426.04, 1977

Highest bioconcentration factor for a single fish species = 6,400

Lowest residue concentration = 0.03 mg/kg

0.03
6400 = 0.0000047 mg/kg or 0.0047 µg/l

Table 13. Other marine data for endrin

<u>Organism</u>	<u>Test Duration</u>	<u>Effect</u>	<u>Result (ug/L)</u>	<u>Reference</u>
American oyster, <u>Crassostrea virginica</u>	4 days	Bioconcentration factor = 1,200		Schimmel, et al. 1975
Grass shrimp, <u>Palaemonetes pugio</u>	4 days	Bioconcentration factor = 830		Schimmel, et al. 1975
Grass shrimp, <u>Palaemonetes pugio</u>	1.5 hrs.	No avoidance	0.1, 1.0, 10	Hansen, et al. 1973
Pink shrimp, <u>Penaeus duorarum</u>	4 days	Bioconcentration factor = 980		Schimmel, et al. 1975
Sheepshead minnow, <u>Cyprinodon variegatus</u>	4 days	Bioconcentration factor = 2,600		Schimmel, et al. 1975
Sheepshead minnow, <u>Cyprinodon variegatus</u>	1.5 hrs.	Avoidance	0.1, 1.0	Hansen, 1969
Sheepshead minnow, <u>Cyprinodon variegatus</u>	1.5 hrs.	No avoidance	0.01, 10	Hansen, 1969
Sheepshead minnow (embryo-juvenile), <u>Cyprinodon variegatus</u>	33 days	LC50	0.16	Schimmel, et al. 1975
Sheepshead minnow (embryo-juvenile), <u>Cyprinodon variegatus</u>	33 days	Bioconcentration factor 3,300 to 4,800		Schimmel, et al. 1975
Mummichog, <u>Fundulus heteroclitus</u>	10 days	LC50	0.33	Eisler, 1970a
Sailfin molly, <u>Poecilia latipinna</u>	4 days	Bioconcentration factor = 2,400		Schimmel, et al. 1975
Spot, <u>Leiostomus xanthurus</u>	8 mos.	Death	0.075	Lowe, 1966
Spot, <u>Leiostomus xanthurus</u>	8 mos.	No effect	0.05	Lowe, 1966
Northern puffer, <u>Sphaeroides maculatus</u>	4 days	Abnormal liver function	0.05	Eisler & Edmunds, 1966

ENDRIN

REFERENCES

- Argyle, R.L., et al. 1973. Endrin uptake and release by fingerling channel catfish, Ictalurus punctatus. Jour. Fish. Res. Board Can. 30: 1743.
- Batterton, J.C., et al. 1971. Growth response of bluegreen algae to aldrin, dieldrin, endrin, and their metabolites. Bull. Environ. Contam. Toxicol. 6: 589.
- Bennett, H.J., and J.W. Day, Jr. 1970. Absorption of endrin by the bluegill sunfish, Lepomis macrochirus. Pestic. Monitor. Jour. 3: 201.
- Brungs, W.A., and G.W. Bailey. 1966. Influence of suspended solids on the acute toxicity of endrin to fathead minnows. Proc. 21st Purdue Ind. Waste Conf., Part 1, 50: 4.
- Butler, P.A. 1963. Commercial fisheries investigations, pesticide-wildlife studies, A review of fish and wildlife service investigations during 1961 and 1962. U.S. Dep. Inter. Fish Wildl. Circ. 167: 11.
- Cutkomp, L.K., et al. 1971. ATPase activity in fish tissue homogenates and inhibitory effects of DDT and related compounds. Chem. Biol. Int. 3: 439.

Davis, H.C., and H. Hidu. 1969. Effects of pesticides on embryonic development of clams and oysters and on survival and growth of the larvae. U.S. Dep. Inter. Fish Wildl. Fish. Bull. 67: 393.

Davis, P.W., et al. 1972. Organochlorine insecticide, herbicide, and polychlorinated biphenyl (PCB) inhibition of NaK-ATPase in rainbow trout. Bull. Environ. Contam. Toxicol. 8: 69.

Earnest, R.D., and P.E. Benville, Jr. 1972. Acute toxicities of four organochlorine insecticides to two species of surf perch. Calif. Fish Game. 58: 127.

Eisler, R. 1969. Acute toxicities of insecticides to marine decapod crustaceans. Crustaceana 16: 302.

Eisler, R. 1970a. Factors affecting pesticide-induced toxicity in an estuarine fish. Tech. Pap. 45. Bur. Sport Fish. Wildl. U.S. Dep. Inter.

Eisler, R. 1970b. Acute toxicities of organochlorine and organophosphorous insecticides to estuarine fishes. Tech. Pap. 46. Bur. Sport Fish. Wildl. U.S. Dep. Inter.

Eisler, R., and P.H. Edmunds. 1966. Effects of endrin on blood and tissue chemistry of a marine fish. Trans. Am. Fish. Soc. 95: 153.

Fabacher, D.L. 1976. Toxicity of endrin and an endrinmethyl parathion formulation to largemouth bass fingerlings. Bull. Environ. Contam. Toxicol. 16: 376.

Ferguson, D.E., et al. 1965. Tolerance of five chlorinated hydrocarbon insecticides in two species of fish from a transect of the lower Mississippi River. Jour. Miss. Acad. Sci. 11: 239.

Ferguson, D.E., and C.R. Bingham. 1966. Endrin resistance in the yellow bullhead, Ictalurus natalis. Trans. Am. Fish. Soc. 95: 325.

Ferguson, D.E., et al. 1966. Dynamics of endrin uptake and release by resistant and susceptible strains of mosquito-fish. Trans. Am. Fish. Soc. 95: 335.

Gauvin, A.R., et al. 1965. The toxicity of ten organic insecticides to various aquatic invertebrates. Water Sewage Works 12: 276.

Grant, B.F., and P.M. Mehrle. 1970. Chronic endrin poisoning in goldfish, Carassius auratus. Jour. Fish. Res. Board Can. 27: 2225.

Grant, B.F., and P.M. Mehrle. 1973. Endrin toxicosis in rainbow trout, Salmo gairdneri. Jour. Fish. Res. Board Can. 30: 31.

Hansen, D.J. 1969. Avoidance of pesticides by untrained sheepshead minnows. Trans. Am. Fish. Soc. 98: 426.

Hansen, D.J., et al. 1973. Avoidance of pesticides by grass shrimp, Palaemonetes pugio. Bull. Environ. Contam. Toxicol. 9: 129.

Hansen, D.J., et al. 1977. Endrin: Effects on the entire life-cycle of saltwater fish, Cyprinodon variegatus. Jour. Toxicol. Environ. Health. 3: 721.

Henderson, C., et al. 1959. Relative toxicity of ten chlorinated hydrocarbon insecticides to four species of fish. Trans. Am. Fish. Soc. 88: 23.

Hermanutz, R. 1978. Endrin and malathion toxicity to flagfish, Jordanella floridae. Arch. Environ. Contam. Toxicol. 7: 159.

Iyatomi, K.T., et al. 1958. Toxicity of endrin to fish. Prog. Fish.-Cult. 20: 155.

Jackson, G.A. 1976. Biologic half-life of endrin in channel catfish tissues. Bull. Environ. Contam. Toxicol. 16: 505.

Jarvinen, A.W., and R.M. Tyo. 1978. Toxicity of fathead minnows of endrin in food and water. Arch. Environ. Contam. Toxicol. 7: 1.

Jensen, L.D., and A.R. Gaufin. 1966. Acute and long-term effects of organic insecticides on two species of stonefly naiads. Jour. Water Pollut. Control Fed. 38: 1273.

Katz, M. 1961. Acute toxicity of some organic insecticides to three species of salmonids and the threespine stickleback. Trans. Am. Fish. Soc. 90: 264.

Katz, M., and G.G. Chadwick. 1961. Toxicity of endrin to some Pacific Northwest fishes. Trans. Am. Fish. Soc. 90: 394.

Korn, S., and R. Earnest. 1974. Acute toxicity of 20 insecticides to striped bass, Morone saxatilis. Calif. Fish and Game. 60: 128.

Lincer, J.L., et al. 1970. DDT and endrin fish toxicity under static versus dynamic bioassay conditions. Trans. Am. Fish. Soc. 99: 13.

Lowe, J.I. 1966. Some effects of endrin on estuarine fishes. Proc. Am. Conf. S.E. Assoc. Game and Fish Comm.

Lowe, J.I. Results of toxicity tests with fishes and macroinvertebrates. Data sheets available from U.S. Environ. Prot. Agency, Environmental Research Laboratory, Gulf Breeze, Florida 32561.

Ludke, J.L., et al. 1968. Some endrin relationships in resistant and susceptible populations of golden shiners, Notemigonus crysoleucas. Trans. Am. Fish. Soc. 97: 260.

Macek, K.J., et al. 1969. Effects of temperature on the susceptibility of bluegills and rainbow trout to selected pesticides. Bull. Environ. Contam. Toxicol. 4: 174.

Mason, J.W., and D.R. Rowe. 1976. Accumulation and loss of dieldrin and endrin in the eastern oyster. Arch. Environ. Contam. Toxicol. 4: 349.

Menzel, D.W., et al. 1970. Marine phytoplankton vary in their response to chlorinated hydrocarbons. Science 167: 1724.

Mount, D.I. 1962. Chronic effects of endrin on bluntnose minnows and guppies. Fish Wildl. Serv. Res. Rep. 58. U.S. Dep. Inter. 38 p.

Mount, D.I., and G.J. Putnicki. 1966. Summary report of the 1963 Mississippi kill. Proc. 31st North Am. Wildl. and Nat. Res. Conf. p. 176.

Naqvi, S.M., and D.E. Ferguson. 1968. Pesticide tolerances of selected freshwater invertebrates. Jour. Miss. Acad. Sci. 14: 121.

Naqvi, S.M., and D.E. Ferguson. 1970. Levels of insecticide resistance in freshwater shrimp, Palaemonetes kadiakensis. Trans. Am. Fish. Soc. 99: 696.

Nebeker, A.F., and A.R. Gaufin. 1964. Bioassays to determine pesticide toxicity to the amphipod crustacean, Gammarus lacustris. Utah. Acad. Proc. 41: 64.

Post, G., and T.R. Schroeder. 1971. Toxicity of four insecticides to four salmonid species. Bull. Environ. Contam. Toxicol. 6: 144.

Sanders, H.O. 1969. Toxicity of pesticides to the crustacean, Gammarus lacustris. Bur. Sport Fish. Wildl. Tech. Pap. 25. U.S. Dep. Inter. 18 p.

Sanders, H.O. 1972. Toxicity of some insecticides to four species of malacostracan crustaceans. Bur. Sport Fish. Wildl. Tech. Paper 66. U.S. Dep. Inter. 19 p.

Sanders, H.O., and O.B. Cope. 1966. Toxicities of several pesticides to two species of cladocerans. Trans. Am. Fish. Soc. 95: 165.

Sanders, H.O., and O.B. Cope. 1968. The relative toxicities of several pesticides to naiads of three species of stoneflies. Limnol. Oceanogr. 13: 112.

Schimmel, S.C., et al. 1975. Endrin: Effects on several estuarine organisms. Proc. 28th Annu. Conf. S.E. Assoc. Game and Fish Comm., 1974. p. 187.

Schoettger, R.A. 1970. Fish-Pestic. Res. Lab., progress in sport fishery research. U.S. Dep. Int. Bur. Sport Fish and Wildl. Res. Publ. 106.

Solon, J.M., et al. 1969. The effect of sublethal concentration of LAS on the acute toxicity of various insecticides to the fathead minnow, Pimephales promelas, Rafinesque. Water Res. 3: 797.

Tyler-Schroeder, D.B. Use of grass shrimp, Palaemonetes pugio, in a life-cycle toxicity test. In Proceedings of a Symposium on Aquatic Toxicology and Hazard Evaluation, eds. L.L. Marking and R.A. Kimerle. Am. Soc. Testing and Materials (ASTM), October 31-November 1, 1977.

U.S. Food and Drug Administration. 1977. Administrative Guidelines Manual 7426.04, Attachment G.

U.S. Food and Drug Administration. 1977. Administrative Guidelines Manual 7426.04, Attachment F.

Vance, B.D., and W. Drummond. 1969. Biological concentration of pesticides by algae. Jour. Am. Water Works Assoc. 61: 360.

Wilson, A.J. 1966. Chem. Assays. Annu. Rep. U.S. Bur. Commercial Fish. Biol. Lab., Gulf Breeze, Fla. Circ. 247: 6.

Mammalian Toxicology and Human Health Effects

Summary

Endrin is the common name of one member of the cyclo-diene group of pesticides. It is a cyclic hydrocarbon having a chlorine-substituted methano bridge structure. Endrin was introduced into the United States in 1951 and is manufactured domestically by the Velsicol Chemical Corporation. The endrin sold in the United States is a technical grade product, containing not less than 95 percent active ingredient, available in a variety of diluted formulations.

Known uses of endrin in the United States are as an avicide, rodenticide, and insecticide, the latter being the most prevalent. The largest single use of endrin domestically is for the control of lepidopteron larvae attacking cotton crops in the southeastern and Mississippi delta states. Thus, endrin enters the environment primarily as a result of direct applications to soil and crops. Waste material discharge from endrin manufacturing and formulating plants and disposal of empty containers also contribute significantly to observed residue levels. In the past several years, endrin utilization has been increasingly restricted, and production has continued to decline. In 1978, endrin production was approximately 400,000 lbs (U.S. EPA, 1978).

Wild and domestic mammals are exposed to endrin primarily through ingestion of treated foliage, although dermal contact and inhalation also occur. Endrin shows little tendency to accumulate in tissues other than adipose tissue; levels of up to 23.7 $\mu\text{g/g}$ have been detected both in internal and external fat of a variety of species following ingestion

of endrin-contaminated feed (Long, et al. 1961).

Metabolism of endrin has been studied extensively in rats. Endrin is readily metabolized in the liver and excreted as hydrophilic metabolites. However, certain toxic metabolites such as 12-ketoendrin (also known as 9-ketoendrin) can be retained for longer periods of time. Rats excrete endrin and its metabolites primarily in the feces; in rabbits, excretion is primarily via the urine.

Endrin is highly toxic to all animals regardless of the route of exposure (Treon, et al. 1955). The primary toxic effect of acute exposure is on the central nervous system. When lethal concentrations are administered to experimental animals, convulsions may occur as soon as 30 minutes after exposure, and may culminate in death through respiratory failure in about 48 hours. The dose lethal to 50 percent of the experimental animals ranges from 3 mg/kg for the monkey to 50 mg/kg for the goat.

Many cases of mammalian fatalities have been reported outside the laboratory. For example, field application of endrin at rates of 0.55 to 2.75 kg/ha resulted in the death of 33 to 100 percent of various species of wild mice inhabiting the target area (Dana and Shaw, 1958).

The chronic toxicity of endrin to mammals is greater than that of other organochlorine pesticides. Sublethal effects in wild animals manifest primarily as behavioral and reproductive disorders, i.e., improper maternal care, temporary loss of normal activity, increased vulnerability to predators, reduced reproductive potential, increased post-natal mortality and fetal death. Chronic exposure

to endrin may also be fatal. Five to eight mg/kg in the diet was fatal to dogs in 18 to 44 days. Twelve mg/kg in the diet for life decreased the survival time for mice. Deer mice succumbed to a diet which contained only 2 mg/kg endrin.

No malignancies attributable to endrin exposure have been reported in the literature; however, endrin has been found to cause chromosomal aberrations in rats following intratesticular injection. Teratogenesis, growth retardation and increases in fetal mortality have been observed in mice and hamsters following endrin administration.

Human exposure to endrin occurs through the diet, from inhalation, and through dermal contact. The average dietary intake in the United States in 1973 was 0.033 $\mu\text{g}/\text{day}$ (0.0005 $\mu\text{g}/\text{kg}/\text{day}$) for a 69.1 kg man. This is far below the maximum daily intake of 138.2 $\mu\text{g}/\text{day}$ (2 $\mu\text{g}/\text{kg}/\text{day}$) established by the World Health Organization. Respiratory and/or dermal exposure to endrin occur during manufacture and distribution but are more likely to result from agricultural uses.

Outbreaks of human poisoning have resulted from accidental contamination of foods and have been traced to doses as low as 0.2 mg/kg body weight. Endrin toxicity seems to result primarily from the effects of endrin and its metabolites on the central nervous system. Symptoms usually observed in victims of endrin poisoning were convulsions, vomiting, abdominal pain, nausea, dizziness, and headache. Respiratory failure was the most common cause of death. Significantly increased activity of the hepatic microsomal drug-metaboliz-

ing enzymes has occurred in individuals employed in the manufacture of endrin. No irreversible adverse effects of occupational exposure to endrin have been reported in the literature so far.

Food contamination by endrin still occurs, but to a constantly decreasing extent. At present, levels are approximately 4,000 times lower than those acceptable to the World Health Organization. Background concentrations in the atmosphere, hydrosphere, and lithosphere, far removed from agricultural areas where endrin is used and industrialized areas where endrin is manufactured, are generally below the levels of detection.

The adverse effects of endrin on fish and wildlife inevitably spread to man. The most direct consequence of endrin applied to the environment is contamination of the human food supply. Humans ingest endrin-treated agricultural produce as well as meat from domesticated and wild animals and fish which feed on contaminated vegetation. Ingestion of 20 mg endrin per day by cows resulted in levels of up to 0.25 $\mu\text{g/g}$ of endrin in milk. Aquatic invertebrates and fish bioconcentrate considerable quantities of endrin from water and pass it on to predatory birds. This contaminated fowl (or the fish themselves) may, in turn, be ingested by humans.

In animals, chronic exposure to endrin may result in damage to the liver, kidneys, heart, brain, lung, adrenal glands, and spleen. Effects secondary to central nervous system disorders have also been observed following chronic

exposure of mammals to sublethal doses of endrin. These include behavioral abnormalities, changes in carbohydrate metabolism, and changes in the composition of the blood. Although no malignancies attributable to endrin have been reported, chromosomal abnormalities and teratogenesis have been induced by endrin in several mammalian species.

EXPOSURE

Ingestion from Water

Occasionally, groundwater may contain more than 0.1 µg/l of endrin, but levels as high as 3 µg/l have been correlated with precipitation and run-off following endrin applications (U.S. EPA, 1978). Drinking water from Franklin, Louisiana, an area of high endrin usage, was found to contain a maximum of 23 ng/l (Laner, et al. 1966).

In a study conducted between March 1964 and June 1967, more than 500 grab samples of finished drinking water and corresponding raw water were collected from ten selected municipal water treatment plants whose source was either the Mississippi or the Missouri Rivers. Of the 458 finished water samples assayed, 156 (34 percent), contained detectable concentrations of endrin. However, the number of finished water samples containing concentrations of endrin in excess of 0.1 µg/l decreased from 23 (ten percent), in the period 1964-1965, to zero, in the period 1966-1967 (Schafer, et al. 1969).

The most recent study of endrin contamination of drinking water was conducted by the U.S. Environmental Protection Agency (1974). Endrin was detected in the finished water from the Carrollton Water Plant in New Orleans, Louisiana. The highest concentration measured from all samples was only 4 ng/l.

Ingestion from Foods

The general population has little exposure to endrin in the diet. In a series of analyses of total diets deter-

mined from "market basket" samples in five regions of the United States, the total average intake from food ranged from approximately 0.009 $\mu\text{g}/\text{kg}$ body weight per day in 1965 to 0.0005 $\mu\text{g}/\text{kg}$ body weight per day in 1970 (Table 1) (Duggan and Lipscomb, 1969; Duggan and Corneliussen, 1972). The six year average intake was 0.005 $\mu\text{g}/\text{kg}$ body weight per day. A market basket consisted of 117 food items grouped into 12 composites required for the 14-day diet for a 16- to 19-year-old male. All foods were treated normally before analysis, i.e., meats were cooked, etc. The average daily intake remained at trace levels throughout the period 1965-1970; however, the frequency of occurrence decreased somewhat (Table 1). The breakdown of endrin levels by food class is given in Table 2.

Processing of some foods before human consumption significantly changed endrin residues. Endrin increased in soybean oils (0.28 ppm) relative to whole crop levels (0.07 ppm) by the extraction process (Hill, 1970; USDA Plant Pest Control Division, 1968). Storage above 12 weeks decreased endrin residues in Irish and sweet potatoes by 20 percent (Solar, et al. 1971). Heat processing and freezing further lowered potato residues 65 and 52 percent, respectively. Studies on turnips (Wheeler, et al. 1969) and carrots (Hermanson, et al. 1970) identified 50 to 80 percent of the endrin in the peels.

Endrin disappearance from growing and harvested crop is so variable that "half-life" data for endrin persistence on food plants should be viewed with skepticism (Hill 1970).

TABLE 1
Average Incidence and Daily Intake of Endrin
(Duggan and Corneliusen, 1972)

Year	Percent positive composites	Daily intake (mg)	mg/kg/body wt/day
1965	2.8	T ^a	0.000009
1966	2.0	T	0.000004
1967	1.7	T	0.000004
1968	1.1	0.001	0.00001
1969	3.3	T	0.000004
1970	1.4	T	0.000005

^aT = Trace, 0.001 mg

TABLE 2
Calculated Daily Intake of Endrin by Food Class (mg/day)^a
(Duggan and Corneliussen, 1972)

Year	Meat, fish, and poultry	Potatoes	Leafy vegetables	Root vegetables	Garden fruit	Oils, fats, shortening
1965	---	T ^b	T	---	---	---
1966	---	T	---	T	T	T
1967	---	T	T	T	---	---
1968	---	T	---	---	---	0.001
1969	T	T	---	---	T	---
1970	---	T	---	T	T	---

^aNo detectable levels were found in dairy products, grains and cereals, legume vegetables, fruits, sugars and adjuncts, or beverages.

^bT=Trace, <0.001 mg/day

The loss of endrin depends on the sum of many factors, including temperature, volatilization, metabolism, and dislodgement by wind and rain. Since generalizations cannot be made that endrin on a given crop will always "disappear" at the same rate, only residue analyses on harvested crops can be ascertained as to potential hazard to humans.

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the nineteen major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

<u>Group</u>	<u>Consumption (Percent)</u>	<u>Weighted Average Percent Lipids</u>
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

Measured steady-state bioconcentration factors were obtained for endrin using six species:

<u>Organisms</u>	<u>BCF</u>	<u>Percent Lipids</u>	<u>Adjusted BCF</u>	<u>Reference</u>
American oyster, <u>Crassostrea virginica</u>	1,670-2,780	1.5	3,303	Mason & Rowe, 1976
American oyster, <u>Crassostrea virginica</u>	1,000	1.5	1,533	Wilson, 1966
Grass shrimp, <u>Palaemonetes pugio</u>	1,490	1.1	3,115	Tyler-Schroeder, In press
Grass shrimp, <u>Palaemonetes pugio</u>	1,600	1.1	3,345	Tyler-Schroeder, In press
Sheepshead minnow, <u>Cyprinodon variegatus</u>	2,500	5.0	1,150	Hansen, et al. 1977
Sheepshead minnow, <u>Cyprinodon variegatus</u>	6,400	5.0	2,944	Hansen, et al. 1977
Spot, <u>Leiostomus xanthurus</u>	1,450	3.1	1,076	Lowe, 1966
Fathead minnow, <u>Pimephales promelas</u>	10,000	8.0	2,875	Mount & Putnicki, 1966
Fathead minnow, <u>Pimephales promelas</u>	7,000	8.0	2,012	Jarvinen & Tyo, 1978
Channel catfish, <u>Ictalurus punctatus</u>	2,000 1,640	3.2	1,302	Argyle, et al. 1973

Each of these measured BCF's was adjusted from the percent lipids of the test species to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. The geometric mean was obtained for each species, and then for all species. Thus, the mean bioconcentration factor for endrin and the edible portion of all aquatic organisms consumed by Americans is calculated to be 1,900.

Because of the dynamic state of endrin in the biological tissues of lower animals (Mount, et al. 1966), the bioaccumulation is short-lived, and tissue burdens diminish rapidly once the environmental source is removed. (Toxic endrin metabolites, such as 12-ketoendrin, may persist for longer periods of time). Commercial catfish from Arkansas and Mississippi were reported to contain average residues ranging from 0.01 to 0.41 $\mu\text{g/g}$. Four percent of the samples exceeded the FDA action level for maximum permissible endrin concentration of 0.3 $\mu\text{g/g}$ in the edible portion of fish (Hawthorne, et al. 1974; Crockett, et al. 1975).

Humans may also be exposed to endrin in cow milk and steer, lamb, and hog meat, however, endrin is so rapidly metabolized and excreted that tissue levels are usually at or below the dietary concentrations of endrin. Residue levels in excess of 0.25 $\mu\text{g/g}$ on a fat basis were detected in the milk of 40 Wisconsin dairy herds between 1964 and 1967 (Moubry, et al. 1968). Endrin was presumably retained in the milk fat for up to four weeks. However, the quantities of endrin ingested during that period were not controlled. Williams and Mills (1964) studied the appearance of endrin in cow's milk under controlled feeding conditions. Endrin concentrations in the milk increased progressively during the first few days of feeding until they plateaued at 13 to 15 days. When ingestion of endrin ceased, residues in milk declined sharply and following 20 days on an endrin-free diet, detectable (greater than 0.001 $\mu\text{g/g}$) levels were present only in milk samples from cows fed the highest levels of endrin (0.3 mg/kg). Endrin is apparently excreted in

milk in higher concentrations when fed as a residue on hay than when fed dissolved in soybean oil (Ely, et al. 1957). However, in general, a total daily endrin intake of greater than 20 mg as a residue sprayed in forage is necessary for excretion of measurable quantities of endrin in milk. In another study (Saha, 1969), the ratio of residue in milk to feed was 0.07.

Studies by Brooks (1969) demonstrated that steers, lambs, and hogs receiving 0.1 mg/kg endrin in the diet for 12 weeks showed little tendency to deposit endrin in body tissues. Continuous feeding of up to 2 mg/kg resulted in a maximum body fat content of 1 $\mu\text{g/g}$. Long, et al. (1961) reported high levels of storage (23.7 $\mu\text{g/g}$) in the adipose tissue of lambs. Higher levels were detected in the internal fat surrounding the stomach and thoracic cavity than in external fat deposits. After the lambs were transferred to untreated pasture, endrin levels in fat decreased somewhat, but levels of approximately 6.4 to 13.8 $\mu\text{g/g}$ were still retained in fat. Pigs receiving 510 mg endrin over 30 days had fat endrin levels of no more than 2 $\mu\text{g/g}$, and no endrin was detected in any other tissue (Brooks, 1974).

Inhalation

Agricultural workers, home gardeners, and those involved in manufacture or distribution of endrin might thus become exposed through inhalation. Respiratory exposure during periods of orchard spraying may generally be expected to reach 0.01 mg/hour (Wolfe, et al. 1963; Wolfe, et al. 1967).

Wolfe, et al. (1963) reported that spraying of potatoes with a one percent solution of endrin dust produced levels of 0.41 mg/hour for respiratory exposure. During the spraying of raw crops the respiratory exposure rate was below the limits of detection of the analytical method employed (Jegier, 1964).

Another possible means of inhalation exposure to endrin is from the residues on tobacco plants used for smoking. Bowery, et al. (1959) found that tobacco retained an average of 0.2 μg of endrin per commercial cigarettes. Forty percent of the residual endrin disappears during the curing process, but the remainder persists throughout the cigarette manufacturing process. Endrin residues in pipe tobacco increased approximately three-fold from 1969 (0.05 $\mu\text{g/g}$) to 1971 (0.114 $\mu\text{g/g}$). Residues of endrin in cigars remained at approximately 0.06 $\mu\text{g/g}$ from 1969 to 1972. Endrin residues in cigarettes decreased from 0.18 $\mu\text{g/g}$ to 0.09 $\mu\text{g/g}$ from 1969 to 1971 (Bowery, et al. 1959; Domanski and Guthrie, 1974).

According to data compiled by the U.S. Environmental Protection Agency, exposure of the general populace to endrin via the air decreased from a maximum level in 1971 at Greeley, Colorado, of 25.6 $\mu\text{g/m}^3$ to a maximum in 1975 of 0.5 $\mu\text{g/m}^3$ at Jackson, Mississippi. None of the monitoring data contained endrin levels consistently near the threshold limit value

of $100 \mu\text{g}/\text{m}^3$ suggested by the American Conference of Governmental Industrial Hygienists for 1971.

Dermal

The most significant occupational dermal exposure to endrin occurs during field applications. During dusting or spray-machine operations, dermal exposure is almost always greater than respiratory exposure. Dermal exposure during orchard spraying is likely to range up to 3 mg/body/hour, for workers wearing standard protective clothing in which 3.15 ft^2 of the body is exposed. Potentially, and probably, the greatest hazard associated with the use of endrin, however, occurs during measuring and pouring the emulsifiable concentrate solution (Wolfe, et al. 1963, 1967).

Of the situations tested, higher levels of exposure occurred during dusting of potatoes with a one percent endrin dust. Levels of up to 18.5 mg/hour for dermal exposure were found (Wolfe, et al. 1963). During the application of endrin to row crops, a dermal exposure of 0.15 mg/hour was noted (Jegier, 1964).

PHARMACOKINETICS

Absorption

Endrin is known to be absorbed through the skin, the membraneous areas of the lungs, and through the lining of the gut, however, the literature reveals no data on the rates of absorption.

Distribution

Humans do not tend to store endrin in significant quantities. No residues were detected in plasma, adipose tissue, or urine of workers occupationally exposed to endrin (Hayes

and Curley, 1968). Measurable levels of endrin have not been detected in human subcutaneous fat or blood, even in those areas where it is used extensively, such as India or the lower Mississippi delta area (Brooks, 1974). Despite its high acute toxicity, endrin is a relatively nonpersistent pesticide in humans. Endrin residues have only been detected in the body tissues of humans immediately after an acute exposure. However, little is known concerning the persistence and toxicity of endrin metabolites.

As a result of acute endrin poisoning, high levels of endrin have been observed in both blood and urine but no endrin has been detected in cerebral spinal fluid according to Cobel, et al. (1967). Endrin-poisoned humans have been reported as having an endrin content as high as 400 $\mu\text{g/g}$ in fat tissue and 10 $\mu\text{g/g}$ in other tissues (Coble, et al. 1967). However, the 400 $\mu\text{g/g}$ value was obtained using a bioassay technique presently regarded as unreliable (Curley, et al. 1970). The 10 $\mu\text{g/g}$ value was determined from a patient who died from repeated exposures to endrin. Much lower values of endrin were obtained from an autopsy of body tissues of victims poisoned by eating endrin-contaminated bread in Saudi-Arabia (Table 3). Blood and urine samples taken from patients 29 to 31 days after the outbreak were uniformly negative for endrin (Curley, et al. 1970). Low blood levels were detected in three humans who recovered after accidental ingestion of endrin. In one case, the concentration of endrin in the blood 30 minutes after convulsions occurred was 0.053 $\mu\text{g/g}$ and 20 hours past convulsions it was recorded at 0.038 $\mu\text{g/g}$. This same patient excreted 0.02

TABLE 3
Endrin Concentrations Found in Victims
of Endrin Poisoning in Saudi Arabia.
(Curley, et al. 1970)

Sample	Endrin concentrations ($\mu\text{g/l}$)
Blood	0.007-0.032
Urine	0.004-0.007
Vomitas	5.24
Tissues (autopsy) from:	
Stomach	0.16
Liver	0.685
Kidney	0.116

$\mu\text{g/g}$ endrin via the urine during the following 24 hours (Coble, et al. 1967).

Richardson, et al. (1967) fed endrin to nine-month old dogs for 128 consecutive days at a level of 0.1 mg/kg body weight per day. Blood concentrations during the experiment ranged from 0.002 to 0./008 $\mu\text{g/g}$. At the termination of the experiment, concentrations in the adipose tissue ranged from 0.3 to 0.8 $\mu\text{g/g}$; heart, pancreas and muscle were at the lower end of this range, while the concentration in the hepatic tissues was 0.077 to 0.085 $\mu\text{g/g}$. The kidneys and lungs had similar concentrations.

The amounts of endrin detected from the tissues of dogs that survived after being fed for approximately six months on diets containing endrin in concentrations of 4 to 8 mg/kg were as follows: 1 $\mu\text{g/g}$ in the fat; 1 $\mu\text{g/g}$ in the liver; and 0.5 $\mu\text{g/g}$ in the kidneys (Treon, et al. 1955).

Metabolism

Endrin is metabolized and excreted more rapidly than other chlorinated hydrocarbon insecticides (Jager, 1970). There is good evidence that endrin is quickly metabolized in mammals (probably in the liver) and excreted as a hydrophilic metabolite.

In vitro studies appear to support the hepatic metabolism of endrin. A metabolite behaving as a mono-hydroxy derivative was produced when endrin was incubated at 30°C for several hours with both rat liver and pig liver microsomes and NADPH (Brooks, 1969). Formation of the derivative was suppressed by sesamex, an inhibitor of microsomal oxidations.

Information regarding the metabolic fate of endrin in vivo is conflicting. Baldwin, et al. (1970) found that endrin is metabolized in the rat to at least three metabolites. One is 9-ketoendrin, which is found in the urine. The other two metabolites are excreted in the feces and have not been found in body tissues. The acute oral LD₅₀ of ketoendrin to rats (62 mg/kg) is higher than that of endrin (25 mg/kg), and the rearrangement would appear to be a detoxication reaction (Brooks, 1969). Oxidation without skeletal rearrangement has been indicated to preponderate in mammals although details remain to be worked out (Brooks, 1974).

However, Bedford, et al. (1975) studied LD₅₀ values based on ten day mortalities for endrin and three of its mammalian metabolites (anti-12-hydroxyendrin, syn-12-hydroxyendrin, and 12-ketoendrin) in rats. The metabolites were all more toxic than the parent compound LD₅₀ values. Rapidity of intoxication, sex differences, and analysis of the brains of rats dosed with the various compounds indicated that 12-ketoendrin may be the acute toxicant in each case. Thus, the oxidative metabolism of endrin may be responsible for its acute toxicity.

Jager (1970) found, in feeding experiments with rats, that females metabolize endrin more slowly than males. When carbon-14 labeled endrin was fed to male and female rats, the males excreted 60 percent of it in the feces within the first 24 hours and the females only 39 percent. Less than one percent was excreted in the urine. Of the total

radioactivity excreted in the feces, 70 to 75 percent occurred in the form of hydrophilic metabolites; the remainder was in unchanged endrin. Twenty-four hours after the last dose, only hydrophilic metabolites were excreted.

Sex differences in the rate of endrin metabolism in rats were also found by Hutson, et al. (1975). Although the major metabolite in both sexes was anti-12-hydroxyendrin, excreted via the bile as the glucuronide, male rats produced the metabolite at a higher rate than did females. A minor metabolite was trans-4,5-dihydroisodrin-4,5-diol. There was a sex difference in the production and excretion of 12-ketoendrin, which was observed as a urinary metabolite in male rats. The major urinary metabolite in female rats was anti-12-hydroxyendrin-o-sulfate. These authors also found the formation of 12-ketoendrin to be directly related to the acute toxicity of endrin.

Excretion

At high dosage levels, excretion of endrin appears to be slower. Body content of endrin declines fairly rapidly after a single dose or when a continuous feeding experiment is terminated. When the exposure to endrin ceases, the concentration in the tissues diminishes rapidly (Brooks, 1969).

Endrin is primarily excreted with the feces, much of it by way of the bile. The liver has been identified as the major excretory organ for endrin in the rat. The amount of radioactivity in the feces of the rat, from intravenously administered carbon-14 labeled endrin, reflects the amount of radioactivity entering the gastrointestinal tract via

the bile (Cole, et al. 1968).

The major metabolite in both male and female rats was anti-12-hydroxyendrin, which was excreted via the bile as the glucuronide (Hutson, et al. 1975), trans-4,5-dihydroisodrin-4,5-diol was a minor biliary metabolite. 12-ketoendrin was observed as the primary urinary metabolite in the male rat; the major urinary metabolite in female rats was anti-12-hydroxyendrin-o-sulfate. Syn-12-hydroxyendrin was not detected.

Cole, et al. (1968) also studied rates of excretion of radio carbon-labeled endrin in whole rats, bile-fistulated rats, and isolated perfused rat livers. Over 90 percent of the excreted radioactivity was found in the feces of the intact animals and in the bile of the fistulated animals. Fifty percent of the radioactive endrin was excreted within the first 24 hours. In the fistulated animals, 50 percent of the endrin radioactivity was excreted in the bile in approximately one hour in the perfused experiments (Cole, et al. 1968).

With the exception of endosulfan, endrin is the least persistent of any of the chlorinated hydrocarbon pesticides in mammals. It is rapidly metabolized and eliminated from vertebrate tissues. Excretion occurs through the milk as well as through the urine and the feces (Brooks, 1974). Endrin metabolites, one of which is known to be several times more toxic than endrin itself, may persist for longer periods of time.

EFFECTS

Acute, Sub-acute, and Chronic Toxicity

Endrin is classified as "very highly hazardous", meaning that any contact with very small amounts of the substance may result in severe systemic toxicity or death (Thompson, 1971). Endrin is the most acutely toxic of the cyclodiene insecticides and yet, except for endosulfan, is least persistent in mammals (Brooks, 1974). Endrin toxicity can be elicited from any route of exposure. When ingested in one dose by rats, endrin is about three times as toxic as aldrin and about 15 times as toxic as DDT (Treon, et al. 1955). Upon intravenous administration to mice, endrin was five times as toxic as dieldrin (Walsh and Fink, 1972).

The onset of endrin toxicity symptoms is rapid. The return to normal among those who survive is also rapid. The recovery from endrin intoxication is faster than from other cyclodiene pesticides (Brooks, 1974).

Symptoms of acute endrin poisoning in mammals clearly indicate that endrin is a neurotoxicant. The first indication of acute endrin poisoning is usually central nervous system excitation as evidenced by hypersensitivity to external stimuli associated with generalized tremors and followed by severe tonic-clonic convulsions (Brooks, 1974). These convulsions may occur as early as 30 minutes after acute endrin exposure (Brooks, 1974). Convulsions can culminate in death from respiratory failure (Brooks, 1974). In the range of the acute oral LD₅₀ (17 to 43 mg/kg), death of rats may result after 48 hours (Boyd and Stefec, 1969).

Other symptoms of acute endrin poisoning include bradycardia (slowed heartbeat), increase in blood pressure, salivation, and body temperature, leukocytosis (increase in number of white blood cells), increased hemoconcentration, decreased blood pH, increased cerebrospinal fluid pressure and cerebral venous pressure, increased renal vascular resistance with decreased renal blood flow and glomerular filtration rate, decrease in catecholamine concentration of the adrenals, and increased levels of circulating epinephrine and norepinephrine (Emerson, et al. 1964; Reins, et al. 1966). Pathological observations of rats from autopsy reveal signs of a stress reaction, degenerative changes in kidneys, liver and brain capillaries and venous congestion, and loss of weight and dehydration of some organs (Boyd and Stefec, 1969).

The symptoms in man include headache, dizziness, abdominal disturbances, nausea, vomiting, mental confusion, muscle twitching, and epileptiform convulsions which may occur suddenly and without prior warning (Brooks, 1974).

Mammalian susceptibility to endrin toxicity varies greatly with age, sex, and species as shown in Table 4. The LD₅₀ values range from 1.37 to 43 mg/kg. Apparently, mice and monkeys are most sensitive, and guinea pigs are more resistant. Rabbits seem to be somewhat more resistant than monkeys to a single dose of endrin. The acute toxicity of endrin is, however, high for all these species.

TABLE 4
Acute Oral Toxicity of Endrin to Mammals

Animal (age, sex)	LD ₅₀ (mg/kg)
Mouse	1.37 ^a
Rats (6 months, M)	43 ^b
Rats (6 months, F)	7 ^b
Rats (30 days, M)	30 ^b
Rats (30 days, F)	17
Rat	3 ^a
Rabbits (F)	7-10 ^b
Hamster	10 ^a
Guinea pigs (F)	16 ^b
Guinea pigs (M)	36 ^b
Monkey	3 ^b

^aNIOSH, 1977

^bTreon, et al. 1955

In rats and guinea pigs, females are more susceptible than males. The greater susceptibility of female rats six months of age, than that of younger female rats is the reverse of the more normal relationship between age and susceptibility found in males.

When endrin was maintained in contact, as a dry 100-mesh, powder, with either intact or abraded skin of female rabbits for 24 hours, the minimum lethal dosage was found to be greater than 60 and less than 94 mg/kg. Poisoned animals had convulsions, but neither gross nor microscopic evidence of damage to the skin was found. Degeneration of the cells in the central zones of the lobules of the livers of rabbits was observed (Treon, et al. 1955).

Graves and Bradley (1965) determined an LD₅₀ of 5.6 mg/kg for endrin injected into the peritoneal cavity of Swiss albino mice. An intravenous LD₅₀ of 2.3 mg/kg was determined by Walsh and Fink (1972) for adult male mice. Endrin injected into dogs intravenously at a dosage of 3 mg/kg resulted in death in approximately 75 percent of the animals (Hinshaw, et al. 1966).

Target organs found in acute experiments are not always the same as those following repeated exposure over long periods of time. The central nervous system is the target of acute endrin poisoning. When an animal is repeatedly exposed to low doses (0.8 to 3.5 mg/kg/day) of endrin, it can often make compensatory adjustments to cope with the initial nervous system injury until damage to liver or other organs intervenes. However, Chernoff, et al. (1979) found

that the threshold level for convulsions in hamsters was 10 mg endrin/kg body weight. This convulsive dose was approximately twice that required for the production of teratogenic effects.

After exposure of rats, rabbits, guinea pigs, cats, dogs, and monkeys to varying doses, routes, and frequencies of administration, diffuse degenerative changes were observed in the livers, kidneys, and brains of all fatally poisoned animals. Tissue alterations were also observed in some of the surviving animals (Treon, et al. 1955). Rabbits subjected to multiple dermal applications (20 to 44 mg/kg) exhibited severe fatty degeneration of the liver (Treon, et al. 1955). A series of 50 oral doses of 1 to 5 mg/kg/day in a rabbit caused diffuse degeneration and fatty vacuolization of the hepatic and renal cells and degeneration of heart tissue. Rabbits that survived 118 periods of inhalation of 0.36 ppm endrin developed a granulomatous type of pneumonitis (Treon, et al. 1955).

Revin (1968) found that chronic administration of endrin can lead to convulsions. He administered endrin to squirrel monkeys at a minimum rate of 0.2 mg/kg/day, which caused a characteristic change in the electroencephalogram (EEG) from relatively small doses -- 0.5 to 1.0 mg/kg. At total doses of 5 to 10 mg/kg, electrographic seizures developed. Endrin administration was stopped after seizures, but after three weeks, EEG's and behavior were still abnormal. Recurrence of seizures, under stress conditions, months after termination of endrin administration demonstrated that even small amounts of endrin stored in the body after

exposure cannot be regarded as toxicologically inert. Endrin, mobilized by stress, may cause toxic responses in the brain. If concentrations in the fat of these monkeys (approximately 25 $\mu\text{g/g}$ after four months) were sufficient to cause seizures, the same stress to an animal storing 2.5 $\mu\text{g/g}$ may induce EEG and, possibly, behavioral changes (Revin, 1968).

The chronic toxicity of endrin is greater than that of other organochlorine pesticides. In prolonged feeding experiments, rats can consume diets containing approximately three times as much aldrin and 12 times as much DDT as endrin without increase in relative weights of specific organs. Dogs are at least 10 times as susceptible to the toxic effects of endrin as to those of DDT (Treon, et al. 1955). Species and sex differences exist in susceptibility to chronic endrin toxicity. Females are generally more susceptible than males. Rabbits and dogs are more susceptible than rats (Treon, et al. 1955).

Mammalian species appear to be sensitive to the toxic effects of endrin at low levels in their diet. Significant mortality during a seven month period appeared in deer mice when fed 2 mg/kg endrin in the diet (Morris, 1968). The deer mice exhibited symptoms of hypertension, uncoordination, muscle tremors, and convulsions which increased in intensity until death occurred.

Endrin fed throughout the life to Osborne-Mendel rats at 12 mg/kg in the diet decreased viability. Mean survival time fell from 19.7 months to 17.6 months for males and from 19.5 months to 18.2 months for females. The endrin-fed rats experienced moderate increases in incidence of

congestion and focal hemorrhages of the lung; slight enlargement, congestion and mottling of the liver; slight enlargement, discoloration or congestion of the kidneys (Deichmann, et al. 1970).

Dogs can tolerate only about half as much endrin in their diet as rats. Dogs, which died when fed toxic concentrations (5 mg/kg or more) of endrin for 18 to 44 days, regurgitated their food, became lethargic, salivated, and subsequently refused to eat. These dogs became emaciated and developed respiratory distress and signs of irritation of the central nervous system. Dogs fed a diet containing endrin (8 mg/kg for six weeks) exhibited enlargement of the liver, kidneys, and brain and reduction in the deposition of free peritoneal and omental fat. After 19 months on diets containing 3 mg/kg endrin, dogs had significantly enlarged kidneys and hearts (Treon, et al. 1955).

Fatally poisoned dogs exhibited diffuse degenerative lesions in the brain, heart, liver, and kidneys, plus pulmonary hyperemia and edema. Severe renal damage was apparent characterized by diffuse degeneration and necrosis of the convoluted tubules. The liver had diffuse degeneration and fatty vacuolization and, in some cases, necrosis of the liver cells (Treon, et al. 1955).

Synergism and/or Antagonism

The acute oral toxicity (LD_{50}) of equitoxic doses of combinations of 15 pesticides was examined by Keplinger and Deichmann (1967). The results are presented in Table 5. Endrin plus diazinon, endrin plus toxaphene, and endrin plus malathion showed additive effects; while endrin plus parathion, endrin plus DDT and, particularly, endrin plus delnav showed lower than expected LD_{50} 's, suggestive of antagonistic effects. Joint administration of endrin and its closely related compound aldrin showed a more than additive effect, and endrin plus chlordane was found to exert a potentiating effect.

TABLE 5

Expected and observed oral LD_{50} 's of Endrin
plus other Pesticides in Mice.
(Keplinger and Deichmann, 1967)

Other Pesticides	Expected LD_{50} (mg/Kg)	Observed LD_{50} (mg/Kg)	Ratio E/0
Chlordane	473	211	2.22
Aldrin	63	34	1.83
Dieldrin	63	50	1.25
Diazinon	93	93	1.00
Malathion	703	820	0.85
Toxaphene	63	77	0.81
Parathion	12	18	0.65
DDT	213	400	0.53
Delnav	87	195	0.44

No other information is available on synergistic and/or antagonistic effects of endrin.

Teratogenicity

Rats and mice were given 0.58 mg endrin/kg body weight four times weekly for a month, and then after a week or more without endrin treatment, the animals were allowed to become pregnant (Nodu, et al. 1972). A reduced survival rate was found in both species. Nine mouse fetuses with club foot were found in the treated group of 177, while only one fetus with club foot was in the control group of 303.

Endrin exerted embryocidal and teratogenic effects on pregnant hamsters. Both soft and skeletal tissue malformations were produced. Single oral doses of endrin (5 mg/kg) administered to pregnant Syrian golden hamsters on day seven, eight, or nine of gestation caused a high incidence of fetal death, congenital abnormalities and growth retardation. Thirty-two percent of the implantations resulted in fetal mortalities. Teratogenic effects were observed in 28 percent of the fetuses from hamsters treated on day eight. Open eye occurred in 22 percent, webbed foot in 16 percent, cleft palate in 5 percent, cleft lip in 1 percent, and fused ribs in 8 percent (Ottolenghi, et al. 1974).

Ottolenghi, et al. (1974) also found endrin to be teratogenic in mice, but frequency and gravity of the defects produced were less pronounced than in the hamsters when a single dose (2.5 mg/kg in mice and 5 mg/kg in hamsters) of half the LD₅₀ was administered. Abnormalities in the mice included open eye and cleft palate.

Golden hamsters, intubated with endrin (0.75 and 1.5 mg/kg) on days 5 to 14 of gestation had less reactive locomotor activity than controls during gestation but not at

weaning (Gray, et al. 1979). The offspring of these dams were tested in open field at 15, 20, 27, 34, and 44 days of age. Fifteen-day-old pups at the 1.5 mg/kg dose were approximately 90 percent more active than controls but this difference disappeared by day 34. Prenatal endrin exposure appeared to have behavioral effects in hamsters and their offspring.

Chernoff, et al. (1979) found that a single dose of endrin administered on pregnancy, day eight, produced meningoencephaloceles at doses above 1.5 mg/kg and fused ribs at doses above 5.0 mg/kg. Open eyes, cleft palates, and webbed feet were not noted. It was suggested that a teratogenic level of endrin in humans could be lower than the levels estimated to cause human convulsions since the conclusive dose in hamsters was approximately twice that required for the induction of terata.

Mutagenicity

Endrin, as well as aldrin and dieldrin, can cause chromosome damage (Grant, 1973). Symptoms of cellular degeneration have been observed in germinal tissue of male albino rats treated with 0.25 mg endrin administered intratesticularly (Dikshith and Datta, 1972). The most conspicuous effects were chromosomal aberrations, including stickiness, bizarre configurations, formation of chromosome fragments, and abnormal restitution of chromosomes. Formation of single and double bridges with acentric fragments was very common, disturbing the normal disjunction of chromosomes and eventually affecting the chromosome complements of the division

products (Dikshith and Datta, 1973). Unequal distribution of chromosomes at anaphase was also observed. Severe cell damage resulted in liquefaction and transformation of the chromatin mass into an amorphous lump (Dikshith and Datta, 1972). These were the only instances reported of mutagenicity related to endrin.

However, chlorinated cyclopentadienes, such as endrin, were suggested to undergo metabolic conversion forming acylating and possibly mutagenic tetrachlorocyclopentadienone. Using mouse liver microsomes for metabolic activation and E. coli K12(343/113) to detect mutagenicity, tetrachlorocyclopentadiene and pentachlorocyclopentadiene were highly mutagenic after metabolic activation, whereas hexachlorocyclopentadiene was not (Goggelman, et al. 1978).

Carcinogenicity

No malignancies attributed to endrin exposure have been reported. Endrin fed to weanling Osborne-Mendel rats for a lifetime at dietary levels of 2, 6, or 12 mg/kg was neither tumorigenic nor carcinogenic (Deichmann, et al. 1970; Deichmann and MacDonald, 1971; Deichmann, 1972).

A recently completed National Cancer Institute bioassay for possible endrin carcinogenicity concluded that endrin was not carcinogenic for Osborne-Mendel rats or for B6C3F1 mice (U.S. Dept. Health, Education, and Welfare, 1979).

CRITERION FORMULATION

Existing Guidelines and Standards

In 1965, maximum permissible levels were assigned to each of the organochlorine compounds based on the "maximum acceptable concentrations" suggested on July 9, 1965, by the subcommittee on Toxicology to the Public Health Service Advisory Committee on Drinking Water Standards (Schafer, et al. 1969). This concentration for endrin was 0.001 ppm. In 1967, the "maximum reasonable stream allowance" for endrin of 0.1 ppb was suggested by Ettinger and Mount (1967) and was accepted as a guideline.

A maximum acceptable level of 0.002 mg/kg body weight/day was established by a Joint FAO/WHO Meeting on Pesticide Residues in Food held in Rome, November, 1972 (FAO, 1973).

A threshold limit value of 100 $\mu\text{g}/\text{m}^3$ was set for atmospheric levels of endrin by the American Conference of Governmental Industrial Hygienists for 1971 (Yobs, et al. 1972). A threshold limit value of 100 $\mu\text{g}/\text{m}^3$ for an eight hour time-weighted average occupational exposure has also been established by the Occupational Safety and Health Administration (U.S. Code of Federal Regulations, 1972).

Toxic pollutant effluent standards (40 CFR Part 129.102) were promulgated by the U.S.E.P.A. These allowed an effluent concentration of 1.5 $\mu\text{g}/\text{l}$ per average working day calculated over a period of one month, not to exceed 7.5 $\mu\text{g}/\text{l}$ in any sample representing one working day's effluent. In addition, discharge is not to exceed .0006 kg per 1,000 kg of production.

Current Levels of Exposure

While no recent data are available on levels of exposure of humans to endrin it appears that the risk of exposure is decreasing because of the decreased usage of the pesticide.

In a survey of over 500 drinking water samples, the number of samples containing concentrations of endrin in excess of 0.1 $\mu\text{g}/\text{l}$, which has been established as a maximum reasonable stream allowance, decreased from 23 in the period

1964-1965 to 0 in the period 1966-1967 (Schafer, et al. 1969). The most recent study found only 4 ng/l in contaminated drinking water (U.S. EPA, 1974).

In a series of analyses of total diets, the average daily intake of endrin remained at trace levels (<0.001 mg) during the period 1965-1970, but the frequency of occurrence decreased considerably (Duggan and Lipscomb, 1969; Duggan and Corneliussen, 1972).

Exposure of the general populace to endrin in the air decreased from a maximum level of $25.6 \mu\text{g}/\text{m}^3$ in 1971 at Greeley, Colorado, to a maximum of $0.5 \mu\text{g}/\text{m}^3$ in 1975 in Jackson, Mississippi, (U.S.EPA, 1971).

Special Groups at Risk

Agricultural workers, home gardeners, and those involved in endrin manufacture and distribution are the most likely to be exposed to endrin. They may be exposed through inhalation or dermal exposure. The most significant occupational exposure comes during spraying of fields, and dermal exposure is almost always greater than respiratory exposure. Probably the greatest hazard associated with the use of endrin occurs when measuring and pouring the emulsifiable concentrate material. Because endrin has been shown to cause teratogenic effects, pregnant women, particularly those whose diets may contain large amounts of fish, must also be considered a special group at risk. Evidence that endrin may cause chromosomal damage in germinal tissue suggests that men and women of child-bearing intent may also be a special risk group.

Endrin concentrations are highest in the atmospheres over agricultural areas and probably reach their peak levels during the pesticide use season. Of all urban communities, those surrounded by farm lands run the highest risk of atmospheric contamination. Endrin absorbed to particulates could not be detected in the air over representative communities but may perhaps be present at very low concentrations in the vapor phase. Urban communities far removed from agricultural areas are unlikely to experience significant contamination. The homes of occupationally exposed workers have higher levels of atmospheric contamination than do those of the general populace.

Basis and Derivation of Criterion

The limited teratogenic and mutagenic studies on endrin suggest that effects are induced with high endrin doses. However, an unusual administration route was used in these studies. Such levels do not occur in water supplies under normal circumstances, therefore, the results of these studies were not used as the basis for the criterion. More toxicological data must be gathered about these potential effects of endrin before a final conclusion can be reached. The available data do not indicate that endrin is carcinogenic.

On the basis of long-term dietary studies in mammals and occupational exposures in man, a realistic drinking water criterion may be proposed. Maximum no-effect dietary levels of endrin reported for experimental animals are:

Species	Dose level (Duration)	Reference
Mouse	1 mg/kg (lifetime)	U.S. EPA. 1973
Rat	1 mg/kg (2 Years)	Treon, et al. 1955
Rat	1 mg/kg (established no-effect level)	Brooks, 1974
Hamster	1.5 mg/kg (no effect level) (one day)	Chernoff, et al. 1979
Dog	0.1 mg/kg (128 days)	Richardson, et al. 1967
Dog	1 mg/kg (established no-effect level)	Brooks, 1974

Extrapolation of the 0.1 mg/kg no-effect dietary level for the dog to man is reasonable. Since experimental studies of chronic human ingestion are not available (but acute exposure data are), and valid long-term animal feeding studies have been done in more than one species, an uncertainty factor of 100 may be used in the absence of any indication of carcinogenicity in arriving at a water criterion. In deriving a water quality criterion, human exposure to endrin was assumed to come from daily ingestion of 2 l of water and 18.7 g of fish with a bioconcentration factor of 1900 for endrin. Using a no-effect dose level of 0.1 mg/kg, the total allowable intake for a 70-kg man is:

$$0.1 \text{ mg endrin/kg} \times 70 \text{ kg} = \frac{7 \text{ mg/day}}{100 \text{ (uncertainty factor)}} = 70 \text{ } \mu\text{g/day}$$

The criterion for endrin is thus:

$$x = \frac{70 \text{ } \mu\text{g/day}}{2/1 + (0.0187 \text{ kg} \times 1900)} = 1.87 \text{ } \mu\text{g/l} \sim 1.9 \text{ } \mu\text{g/l}$$

This approximates closely the 1 $\mu\text{g}/\text{l}$ maximum allowable concentration for endrin proposed by the Public Health Service for drinking water. It is therefore, recommended that the endrin criterion be established at 1 μg endrin/l of ambient water (1 ppb).

This calculation assumes that 100 percent of man's exposure is assigned to the ambient water pathway. Although it is desirable to establish a criterion based upon total exposure potential, the data for other exposure conditions have not been factored into this analysis.

In summary, based upon the use of toxicologic data for dogs, and an uncertainty factor of 100, the initial level for endrin corresponding to daily intake of 70 $\mu\text{g}/\text{day}$, is 1.9 $\mu\text{g}/\text{l}$. Since the existing 1 $\mu\text{g}/\text{l}$ allowable concentration in the drinking water standards is reasonably close to 1.9 $\mu\text{g}/\text{l}$, it is recommended that 1.0 $\mu\text{g}/\text{l}$ be used as the criterion with notation that there are special groups at risk.¹ Drinking

¹If endrin was present in waters from which edible fish were located and if these fish concentrate endrin by a factor of 1900, this criterion may not be sufficient to protect a special high risk group (i.e., pregnant women who consume a single dose of endrin contaminated fish). Given the bioconcentration factor, fish in water at the maximum recommended concentration of 1 $\mu\text{g}/\text{l}$, may contain 1.9 $\mu\text{g}/\text{g}$ endrin. A 250/g portion of fish would contain approximately 0.5 mg endrin (or 0.01 mg/kg for a 50/kg female). This dose provides a margin of safety of only 150 over the NOEL of 1.5 mg/kg for teratogenicity in the hamster (Chernoff, et al. 1979). The adequacy of this margin of safety is highly questionable, especially given the likelihood of consumption of more than 250/g of fish at a given time. The recommended water quality criterion of 1 $\mu\text{g}/\text{l}$ was based on a chronic exposure study, teratologic outcomes are more likely to occur with acute exposures at critical times in gestation.

water contributes five percent of the assumed exposure while eating contaminated fish products accounts for 95 percent.

The criterion level for endrin can alternatively be expressed as 1.1 $\mu\text{g/l}$ if exposure is assumed to be from the consumption of fish and shellfish alone.

REFERENCES

- Argyle, R.L., et al. 1973. Endrin uptake and release by fingerling channel catfish, Ictalurus punctatus. Jour. Fish Res. Board Can. 30: 1743.
- Baldwin, M.K., et al. 1970. Metabolism of endrin in the rat. Jour. Agric. Food Chem. 18: 1117.
- Bedford, C.T., et al. 1975. The acute toxicity of endrin and its metabolites to rats. Toxicol. Appl. Pharmacol. 33: 115.
- Bowery, T.G., et al. 1959. Insecticide residues on tobacco. Jour. Agric. Food Chem. 7: 693.
- Boyd, E.M., and I. Stefec. 1969. Dietary protein and pesticide toxicity with particular reference to endrin. Can. Med. Assoc. Jour. 101: 335.
- Brooks, G.T. 1969. The metabolism of diene-organochlorine (cyclodiene) insecticides. Residue Rev. 28: 81.
- Brooks, G.T. 1974. Chlorinated insecticides. Vol. II: Biological and environmental aspects. CRC Press, Cleveland, Ohio.
- Chernoff, N., et al. 1979. Perinatal toxicity of endrin in rodents. I. Fetotoxic effects of prenatal exposure in hamsters. Manuscript submitted to Toxicol. Appl. Pharmacol. and the U.S. Environ. Prot. Agency.

- Cobel, Y., et al. 1967. Acute endrin poisoning. Jour. Am. Med. Assoc. 202: 153.
- Cole, J.F., et al. 1968. Endrin and dieldrin: A comparison of hepatic excretion rates in the rat. (Abstr.) Toxicol. Appl. Pharmacol. 12: 298.
- Cordle, F., et al. 1978. Human exposure to polychlorinated biphenyls and polybrominated biphenyls. Environ. Health Perspect. 24: 157.
- Crockett, A.B., et al. 1975. Pesticide and mercury residues in commercially grown catfish. Pestic. Monitor. Jour. 8: 235.
- Curley, A., et al. 1970. Measurement of endrin following epidemics of poisoning. Bull. Environ. Contam. Toxicol. 5: 25.
- Dana, R.H., and D.H. Shaw. 1958. Meadow mouse control in holly. Calif. Dep. Agric. Bull. 47: 224.
- Deichmann, W.B. 1972. Toxicology of DDT and related chlorinated hydrocarbon pesticides. Jour. Occup. Med. 14: 285.
- Deichmann, W.B., and W.E. MacDonald. 1971. Organochlorine pesticides and human health. Food Cosmet. Toxicol. 9: 91.
- Deichmann, W.B., et al. 1970. Tumorigenicity of aldrin, dieldrin, and endrin in the albino rat. Ind. Med. Surg. 39: 37.

DHEW. 1979. Bioassay of endrin for possible carcinogenicity.
HEW Pub. No. (NIH) 79-812. National Cancer Institute, U.S.
Dept. of Health, Education and Welfare, Bethesda, Md.

Dikshith, T.S.S., and K.K. Datta, 1972. Effect of intratesticular injection of lindane and endrin on the testes of rats. *Acta Pharmacol. Toxicol.* 31: 1.

Dikshith, T.S.S., and K.K. Datta. 1973. Endrin induced cytological changes in albino rats. *Bull. Environ. Contam. Toxicol.* 9: 65.

Domanski, J.J., and F.E. Guthrie. 1974. Pesticide residues in 1972 cigars. *Bull. Environ. Contam. Toxicol.* 11: 312.

Duggan, R.E., and G.Q. Lipscomb. 1969. Dietary intake of pesticide chemicals in the United States (II), June 1966-April 1968. *Pestic. Monitor. Jour.* 2: 153.

Duggan, R.E., and P.E. Corneliussen. 1972. Dietary intake of pesticide chemicals in the United States (III), June 1968-April 1970. *Pestic. Monitor. Jour.* 5: 331.

Ely, R.E., et al. 1957. Excretion of endrin in the milk of cows fed endrin-sprayed alfalfa and technical endrin. *Jour. Ecom. Entomol.* 50: 348.

Emerson, T.E., et al. 1964. Cardiovascular effects of the insecticide endrin. *Can. Jour. Physiol. Pharmacol.* 42: 41.

Ettinger, M.B., and D. I. Mount. 1967. A wild fish should be safe to eat. Environ. Sci. Technol. 1: 203.

Food and Agriculture Organization of the United Nations. 1973. 1972 evaluation of some pesticide residues in food. FAO Agricultural Studies No. 90.

Gish, C.D. 1970. Organochlorine insecticide residues in soils and soil invertebrates from agricultural lands. Pestic. Monitor. Jour. 3: 241.

Goggelman, W., et al. 1978. Mutagenicity of chlorinated cyclopentadienes due to metabolic activation. Biochem. Pharmacol. 27: 2927.

Grant, W.F. 1973. Cytological effects of environmental mutagens-pesticides. Mutat. Res. 21: 221.

Graves, J.B., and J.R. Bradley. 1965. Response of Swiss Albino mice to intraperitoneal injection of endrin. Jour. Econ. Entomol. 58: 178.

Gray, L.E., et al. 1979. The effects of endrin administration during gestation on the behaviour of the golden hamster. Abstracts from the 18th Ann. Meet. Soc. of Tox. New Orleans p. A-200.

Hansen, D.J., et al. 1977. Endrin: Effects on the entire lifecycle of saltwater fish, Cyprinodon variegatus. Jour. Toxicol. Environ. Health 3: 721.

Hawthorne, J.C., et al. 1974. Residues of mirex and other chlorinated pesticides in commercially raised catfish. Bull. Environ. Contam. Toxicol. 11: 258.

Hayes, W.J., and A. Curley. 1968. Storage and excretion of dieldrin and related compounds. Arch. Environ. Health 16: 155.

Hermanson, H.P., et al. 1970. Effects of variety and maturity of carrots upon uptake of endrin residues from soil. Jour. Econ. Entomol. 63: 1216.

Hill, K.R. 1970. IUPAC Commission on Terminal Residues. Jour. Assoc. Off. Anal. Chem. 54: 1316.

Hinshaw, L.B., et al. 1966. Effects of the insecticide endrin on the cardiovascular system of the dog. Jour. Pharmacol. Exp. Ther. 153: 225.

Hutson, D.H., et al. 1975. Detoxification and bioactivation of endrin in the rat. Xenobiotica 11: 697.

Jager, K.W. 1970. Aldrin, dieldrin, endrin, and telodrin. Elsevier Publishing Co., Amsterdam.

Jarvinen, A.W., and R.M. Tyo. 1978. Toxicity to fathead minnows of endrin in food and water. Arch. Environ. Contam. Toxicol. 7: 409.

Jegier, Z. 1964. Health hazards in insecticide spraying of crops. Arch. Environ. Health 8: 670.

Keplinger, M.L., and W.B. Deichmann. 1967. Acute toxicity of combinations of pesticides. Toxicol. Appl. Pharmacol. 10: 586.

Laner, G.J., et al. 1966. Pesticide contamination of surface water by sugar cane farming in Louisiana. Trans. Am. Fish. Soc. 95: 310.

Long, W.H., et al. 1961. Endrin residues in the fat of lambs grazed on endrin-treated pasture. Jour. Econ. Entomol. 54: 605.

Lowe, J.I. 1966. Some effects of endrin on estuarine fishes. Proc. 19th Annual Conf. S.E. Assoc. Game and Fish Comm. p. 271.

Mason, J.W., and D.R. Rowe. 1976. Accumulation and loss of dieldrin and endrin in the eastern oyster. Arch. Environ. Contam. Toxicol. 4: 349.

Morris, R.D. 1968. Effects of endrin feeding on survival and reproduction in the deer mouse, Peromyscus maniculatus. Can. Jour. Zool. 46: 951.

Moubry, R.J., et al. 1968. Residues in food and feed. Rate of decline of chlorinated hydrocarbon pesticides in dairy milk. Pestic. Monitor. Jour. 2: 72.

Mount, D.I., et al. 1966. Endrin: Use of concentration in blood to diagnose acute toxicity to fish. Science 152: 1388.

Mount, D.I., and G.J. Putnicki. 1966. Summary report of the 1963 Mississippi kill. Proc. 31st North Am. Wildl. Nat. Res. Conf. p. 176.

National Institute of Occupational Safety and Health. 1977. Registry of toxic effects of chemical substances. DHEW Pub. No. 78-104-A. U.S. Dept. of Health, Education and Welfare, Cincinnati, Ohio.

Nodu, et al. 1972. Influence of pesticides on embryos. On the influence of organochloric pesticides (in Japanese) Oyo Yakuri 6: 673.

Ottolenghi, A.D., et al. 1974. Teratogenic effects of aldrin, dieldrin, and endrin in hamsters and mice. Teratology 9: 11.

Reins, D.S., et al. 1966. Effect of endrin on venous return and catecholamine release in the dog. Can. Jour. Physiol. Pharmacol. 44: 59.

Revin, A.M. 1968. Effects of chronic endrin administration on brain electrical activity in the squirrel monkey. Fed. Prac. 27: 597.

Richardson, L.A., et al. 1967. Relationship of dietary intake to concentration of dieldrin and endrin in dogs. Bull. Environ. Contam. Toxicol. 2: 207.

Saha, J.G. 1969. Significance of organochlorine insecticide residues in fresh plants as possible contaminants of milk and beef products. Residue Rev. 26: 89.

Schafer, M.L., et al. 1969. Pesticides in drinking waters from the Mississippi and Missouri Rivers. Environ. Sci. Technol. 3: 1261.

Sidwell, V.D., et al. 1974. Composition of the edible portion of raw (fresh or frozen) crustaceans, finfish, and mollusks. I. Protein, fat, moisture, ash, carbohydrate, energy value, and cholesterol. Mar. Fish. Rev. 36: 21.

Solar, J.M., et al. 1971. Removal of aldrin, heptachlor epoxide, and endrin from potatoes during processing. Jour. Agric. Food Chem. 19: 1008.

Thompson, A.R. 1973. Pesticides residues in soil invertebrates. In: Environmental Pollution by Pesticides, C.A. Edwards, ed. Plenum Press, New York, Chapt. 3.

Thompson, F.B. 1971. Insecticides II. Toxicity hazards.
N.Z. Jour. Agric. 4: 84.

Treon, J.F., et al. 1955. Toxicity of endrin for laboratory
animals. Agric. Food Chem. 3: 842.

Tyler-Schroeder, D.B. Use of grass shrimp, Palaemonetes
pugio, in a life-cycle toxicity test. In: Proceedings of
a Symposium on Aquatic Toxicology and Hazard Evaluation.
L.L. Marking and R.A. Kimerle, eds. Am. Soc. Testing and
Materials (ASTM), October 31-November 1, 1977. (In press).

U.S. EPA. 1971. Pesticide residues in ambient air, 1971.
Division of Pesticide Community Studies, Chamblee, Ga.

U.S. EPA. 1973. Aspects of pesticidal use of endrin on man
and the environment. Office of Toxic Substances, Washington,
D.C.

U.S. EPA. 1974. Draft analytical report--New Orleans area
water supply study. Lower Mississippi River facility, Surveil-
lance and Analysis Division, Region VI, Dallas, Texas.

U.S. EPA. 1978. Endrin-Position Document 2/3. Special Pesti-
cide Review Division. Office of Pesticide Programs, Washing-
ton, D.C.

Walsh, G.M., and G.B. Fink. 1972. Comparative toxicity and distribution of endrin and dieldrin after intravenous administration in mice. Toxicol. Appl. Pharmacol. 23: 408.

Wheeler, W.B., et al. 1969. Residues of endrin and DDT in turnips grown in soil containing these compounds. Pestic. Monitor. Jour. 3: 72.

Williams, S., and P.A. Mills. 1964. Residues in milk of cows fed rations containing low concentrations of five chlorinated hydrocarbon pesticides. Jour. Assoc. Off. Anal. Chem. 47: 1124.

Wilson, A.J. 1966. Chem. Assays. Annu. Rep. Bur. Commercial Fisheries Biol. Lab., Gulf Breeze, Fla. U.S. Bur. Commercial Fish. Circ. 247: 6.

Wolfe, H.R., et al. 1963. Health hazards of the pesticides endrin and dieldrin. Arch. Environ. Health. 6: 458.

Wolfe, H.R., et al. 1967. Exposure of workers to pesticides. Arch. Environ. Health. 14: 622.

Yobs, A.R., et al. 1972. Levels of selected pesticides in ambient air of the United States. Presented at the National American Chemical Society--Symposium of Pesticides in Air. Boston, Maine.